EXHIBIT D

DOFETILIDE IND-35,009
DOFETILIDE NDA-20,931
BRIEF DESCRIPTION OF REPRESENTATIVE MAJOR ACTIVITIES
DURING THE REGULATORY REVIEW PERIOD

DATE	ACTIVITY	COMMENTS
		DOFETILIDE IND-35,009
6/28/90	Submission to FDA	Initial IND Subm: Protocol 104: An Open Label Dose Titration Study of Orally Administered UK-68,798 in Patients with Sustained Ventricular Tachycardia; Reference IND-33,984 for Pharmacology/Toxicology & Prior Human Experience
7/06/90	Letter from FDA	Assigning IND 35,009
7/31/90	Submission to FDA	Re 7/27/90 telecon with Conrad requesting further information re 104-506: CRF's for 104-506; Expected Risks; IRB Approval & ICF to be submitted as soon as available.
10/04/90	Letter from FDA	Recommendations & Requests: ICF for 104-506; Inert ingredients/stability/specifics for dosage form
10/12/90	Submission to FDA	Safety Report; Letter to investigator; Investigator's Brochure addendum; ICF addendum
10/16/90	Submission to FDA	Re 7/27/90 telecon with Conrad, 7/31/90 Subm - Request for 104-506 IRB Approval/ICF
10/22/90	Telecon	Chen requested revised ICF & ltr to investigators re study 220-021
1/14/91	Submission to FDA	Re 10/04/90 Letter: Response to Division re chemistry; Re 10/22/90 Telecon with Conrad: Chen requested revised ICF addendum
1/25/91	Submission to FDA	Annual Report per 21 CFR 312.33
2/22/91	Submission to FDA	Updated Investigator's Brochure; New protocol 115-106: A Randomized, Double-Blind, Placebo-Controlled Evaluation of the Activity and Safety of Intravenously administered UK-68,798 in Patients with the Wolff-Parkinson-White Syndrome"; New investigators 106, 107; 21 CFR 312.30/.31
4/05/91	Submission to FDA	Protocol 104 modification; Additional investigator to protocol 104; Manufacturing
5/02/91	Submission to FDA	Safety Report per 21 CFR 312.32
5/8/91	Submission to FDA	Investigator's Brochure
5/14/91	Submission to FDA	Protocol 105: Randomized Double-Blind Placebo-Controlled Evaluation of Hemodynamic & Electrophysiologic Effects of 2 Different Oral Doses of UK-68,798 in Patients with Non-Sustained or

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		Sustained Ventricular Tachycardia & Impaired Left Ventricular Function
5/20/91	Submission to FDA	Re 4/03/91 subm to IND-33,984: Adverse electrophysiological events in 5 patients in protocol 107
6/04/91	Submission to FDA	Re 3/19/91 telecon with Chen: Highlighted copy of revised Investigator's Brochure pages
6/14/91	Submission to FDA	Additional investigator to protocol 104
7/08/91	Submission to FDA	Protocol 111: A Randomized Double-Blind Placebo-Controlled Evaluation of the Efficacy and Safety of Orally Administered Dofetilide (UK-68,798) in Patients with Hypertrophic Cardiomyopathy and Paroxysmal Atrial Fibrillation or Flutter
7/12/91	Submission to FDA	Additional investigators to protocol 104; Preclinical
7/26/91	Submission to FDA	Annual Report under 21 C.R.F. 312.33: Re 7/22/91 agreement with Conrad: Combined APR to be submitted on 11/89 anniversary
7/27 & 7/28/91	Telecon	Request for IRB approval, ICF and Case report forms for initial oral study
8/09/91	Submission to FDA	Additional investigators to protocol 104
10/04/91	Submission to FDA	Additional investigators to protocol 104; 1572-Form modifications; Manufacturing
11/01/91	Submission to FDA	Protocol 104 modification; Additional investigator to protocol 104
11/21/91	Submission to FDA	Additional investigator to protocol 104; 1572-Form modification; Manufacturing
12/11/91	Submission to FDA	Protocol 111 modification
12/20/91	Submission to FDA	Additional investigator to protocol 104
1/17/92	Submission to FDA	Additional investigator to protocols 104 & 105
1/22/92	Submission to FDA	Safety Report
1/22/92	Submission to FDA	Protocol 104 modification
2/13/92	Submission to FDA	Annual Report per 21 C.R.F. 312.33; Stability Data
2/17/92	Submission to FDA	Additional investigators to protocols 104 & 105; 1572-Form modifications

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2/21 & 2/28/92	Telecons	Schedule meeting 4/8/92 re development program
2/28/92	Submission to FDA	Protocol 114: Randomized Double-Blind Parallel Placebo-Controlled Evaluation of Orally Administered Dofetilide in Patients with Paroxysmal Atrial Fibrillation or Flutter (PAF) New Investigator; Investigator Brochure (2/92) Manufacturing
3/12/92	Telecon	Reschedule meeting for 4/22/92 (Agenda: Clinical Development Program for Dofetilide)
3/19/91	Telecon	Discuss protocol 107 electro-physiologic events
3/25/92	Submission to FDA	Re 4/22/92 meeting: List of Pfizer attendees, list of consultants, agenda
4/07/92	Submission to FDA	Re 4/22/92 meeting with Division: Agenda & pre-meeting information package
4/10/92	Submission to FDA	Additional investigator to protocol 104; Manufacturing
4/22/92	Meeting	Proposed program for chronic atrial fibrillation & ventricular arrhythmias
5/06/92	Submission to FDA	Additional investigators to protocol 114
5/08/92	Submission to FDA	Meeting minutes of 4/22/92
5/08/92	Submission to FDA	Information Amendment to IND - Clinical, per 21 CFR 312.31
5/12/92	Telecon	Further discussion of atrial fibrillation program
5/20/92	Informal Contact during professional symposium	Lipicky & Friedrich discussion on boosting the event rate in large low dose anticoagulation trials
5/26/92	Telecon	Friedrich/Ryder/Shaw & Chen discuss sudden death of patient in 115-109
6/02/92	Submission to FDA	Safety Report per 21 CFR 312.32
6/04/92	Submission to FDA	Additional investigators to protocol 114; Manufacturing
6/18/92	Telecon	To inform FDA of a patient death
6/30/92	Submission to FDA	Protocol 114C: Long-Term Open-Label Evaluation of Orally Administered Dofetilide Versus Digoxin in Patients Who Relapse into Paroxysmal Atrial Fibrillation or Flutter in Study 115-114; Additional

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		investigators to protocols 114C & 114; Sample Packaging; Manufacturing
7/13/92	Telecon	Follow-up on request for minutes of 4/22/92 "Mid-Phase II" meeting
7/15/92	Submission to FDA	Information Amendment Pharmacology/Toxicology per 21 CFR 312.31; Update division on the status of our preclinical studies in the beagle dog & to seek agreement with our plans
7/31/92	Letter from FDA	Division summary of 4/22/92 meeting
8/04/92	Submission to FDA	Protocol 114A: Long-Term Extension of Double-Blind Treatment for Those Patients Not Experiencing An Attack of Paf in Study 115-114; Additional investigator to protocol 114A
8/05/92	Submission to FDA	Protocols 104, 105, 114 modifications
8/06/92	Submission to FDA	Protocol 114C modification
8/10/92	Submission to FDA	Safety Report per CFR 312.32 (re: Sudden death of patient 115-109-505-0001) per 21 CFR 312.30 and 312.31
8/17/92	Submission to FDA	Additional investigator to protocol 114
9/14/92	Submission to FDA	Additional investigators to protocols 114 & 114C; Manufacturing
9/21/92	Telecon	Clarification re protocol 114A (Chen/Stein)
9/30/92	Submission to FDA	Protocol 111 modification per 21 CFR 312.30
10/1/92	Telecon	FDA requires one-year toxicology dog study (Conrad/Stein)
10/05/92	Submission to FDA	Additional investigators to protocols 114 & 114C CFR 312.30
10/15/92	Letter from FDA	Ref 7/15/92 Submissions; Require 12-Month Toxicology Studies in Dogs
10/23/92	Submission to FDA	Protocol 108B: An Open-Label Long-Term Extension Study of Orally Administered Dofetilide in Patients with Atrial or Ventricular Tachycardia Having Previously Completed Other Dofetilide Studies. Protocol 113: A Randomized Double-Blind Study of Orally Administered Dofetilide and Placebo in Patients with

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		an Implanted Arrhythmia Control Device per 21 CFR 312.30
11/13/92	Telecon	Discuss occurrence of proarrhythmic events (Friedrich/Mehta/Shaw/Stein/Chen)
11/24/92	Submission to FDA	Additional investigators to protocol 113 per 21 CFR 312.30
12/14/92	Submission to FDA	Safety Report per 21 CFR 312.32 - Torsades De Pointes & other proarrhythmic events; Decision to terminate protocol 114
12/18/92 & 1/6/93	Telecon	To inform FDA of a sudden death in 115-399 (Shaw/Stein/Friedrich/Chen)
12/23/92	Submission to FDA	Additional investigators to protocols 113, 114, 114A & 114C; Preclin. & Manufacturing per 21 CFR 312.30/.31
1/14/93	Submission to FDA	Safety Report per 21 CFR 312.32; two sudden deaths in 115-399; Updated risk section of IB
1/21/93	Submission to FDA	New Protocol 003: The Effect of Increased Gastric PH on the Relative Bioavailability of Dofetilide 21 CFR 312.30
1/29/93	Submission to FDA	Additional investigators to protocols 105 & 113 21 CFR 312.30
1/29/93	Telecon	FDA requests notification of sudden cardiac deaths on a quarterly basis and summary in APR. (Conrad/Stein)
2/17/93	Telecon	Requesting waiver from FDA's reminder letter for delayed APR
3/10/93	Submission to FDA	Re 4/22/92 Meeting: Request for meeting to discuss proposed program; Draft protocol 400; Overview of phase III program; 21 CFR 312.47
3/15/93	Submission to FDA	Additional investigators to protocols 108B & 113; Manufacturing, 21 CFR 312.30/.31
4/9/93	Submission to FDA	Protocol 001: Kinetic and Dynamic Interaction Between Dofetilide and Verapamil Under Steady-State Conditions in Healthy Volunteers; Manufacturing; 21 CFR 312.30/.31
4/9/93	Meeting	Topic: Adequacy of study design for the Sudden Unexpected Cardiac Death (SUCD) protocol
4/15/93	Facsimile from FDA	Comments re protocol 001

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5/4/93	Submission to FDA	Additional investigators to protocols 108B & 113; 4/9/93 meeting minutes & overhead presentation; 399-011-0005 SUCD narrative
5/7/93	Submission to FDA	Annual Report under 21 CFR 312.33; Preclinical ; Stability
5/10/93	Submission to FDA	Protocol 002: An Open Study to Compare the Safety Toleration Pharmacokinetics and Pharmacodynamics of Oral Dofetilide in Patients With Chronic Hepatic Insufficiency and in Healthy Subjects Without Hepatic Impairment. Protocol 004: An Observer-Blind Placebo Controlled Parallel Group Study of the Effect of Cimetidine on the Pharmacokinetics and Pharmacodynamics of Dofetilide After Multiple Dosing
5/25/93	Submission to FDA	Protocol 113 amendment: down-titration, other devices allowed, non-thoracotomy leads, clarification of PK times
6/3/93	Submission to FDA	Protocol 120: A Double-Blind, Placebo-Controlled, Multicenter Study Evaluating the Efficacy and Safety of Different Oral Dose Levels of Dofetilide in the Prevention of Recurrence of Atrial Fibrillation/Flutter in Patients with Chronic Persistent Atrial Fibrillation/Flutter Converted Electrically or Pharmacologically to Sinus Rhythm, Additional investigators to protocol 120
6/15/93	Telecon w/ FDA	Roeder (temp CSO) referenced 6/3/93 submission (120); Chen (medical reviewer) has asked for statistician input at FDA but there are no safety issues. FDA told study has started, & Roeder stated there were no issues to hold-up the program
6/25/93	Letter from FDA	Ref 6/3/93 submission (120): Suggest details of recurrence monitoring be specified to "assure sensitivity" of event detection, statistical review ongoing
6/25/93	Telecon w/FDA	Ref 6/3/93 sub 120: Roeder called by Lipicky's req to emphasize importance of recommendation in letter coming from Lipicky re details of monitoring method for recurrence of arrhythmia between visits; lack of action may cause probs w/ evaluation of study
6/25/93	Facsimile from FDA	FDA Facsimiled copy 6/25/93 letter

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6/30/93	Submission to FDA	Amendment to 108B (limits maximum total daily dose for future pts); additional investigators 113, 120; manufacturing info, 399-011 SUCD narrative (pt 0007)
7/15/93	Telecon w/FDA	Ref 6/25/93 letter: FDA response to Pfizer req to meet-OK for telecon w/Chen to discuss 120 comments; Pfizer also wanted to discuss 113; Lipicky available?
7/16/93	Telecon w/FDA	Discussed meeting at FDA vs telecon, Lipicky req'd review material re: discussion topics, will decide forum; Facsimile coming from FDA biometrics
7/16/93	Facsimile from FDA	Reference submission 6/3/93: statistician's comments re: 120 interim analysis (ref. 6/3/93 sub)
7/20/93	Facsimile to FDA	Information Package to Lipicky (ref telecons 7/15-16/93); proposed topics; confirmation of scheduled telecon
7/22/93	Telecon w/FDA	Agenda: protocol design in Chronic AF and life-threatening arrhythmia programs. re: 120- Lipicky letter 6/25 a "suggestion", not requirement; discussed method of determining "benefit" options (UP visits, TTM). re: 113- difficult to get pt numbers; consider proposed study 125 (non-recording ICD study w/lg pt numbers); Lipicky: if 113 looks positive and second study supportive, although "fuzzy", should be sufficient for claim
8/5/93	Submission to FDA	Protocol 006-5001: An Observer-Blind, Placebo-Controlled, Parallel Group Study to Investigate the Effect of Orally Administered Dofetilide on the Pharmacokinetics of Phenytoin in Normal Volunteers, generic labels
8/11/93	Submission to FDA	Additional investigators to protocol 113,120; manufacturing info
8/12/93	Submission to FDA	Protocol 008-9599: An Observer-Blind, Placebo-Controlled, Parallel Group Study to Investigate the Effect of Orally Administered Theophylline on the Pharmacokinetics and Pharmacodynamics of Dofetilide in Normal Volunteers
8/16/93	Submission to FDA	120 amendment: Wafarin adjusted per local practice, add symptom questionnaires (ref 6/25, 7/16/93 letters and 7/22/93 telecon re 120), clarification re: interim analysis, QT/QTc use throughout protocol.
8/16/93	Submission to FDA	Protocol 007-5001: An Observer-Blind, Placebo-Controlled, Parallel Group Study to Investigate the

DATE	ACTIVITY	COMMENTS
		Effect of Orally Administered Phenytoin on the Pharmacokinetics and Pharmacodynamics of Dofetilide in Normal Volunteers, generic labels
8/20/93	Submission to FDA	Protocol 009-9599: An Observer-Blind, Placebo-Controlled, Parallel Group Study to Investigate the Effect of Orally Administered Dofetilide on the Pharmacokinetics and Pharmacodynamics of Theophylline in Normal Volunteers.
8/27/93	Telecon w/FDA	Ref 120 mod (8/16/93): Roeder: Chen/Lipicky prefer TTM at this time (Chen only on 7/22, but Lipicky had indicated UP visit assessments were reasonable). Pfizer requested confirmation.
9/1/93	Telecon w/FDA	Roeder: confirmed Lipicky preferred TTM but study may proceed.
9/2/93	Submission to FDA	002 Amendment: Down-titration, PK contact revised, serious A/E reporting
9/21/93	Submission to FDA	009 Amendment: additional blood sampling to evaluate relationship of EKG changes to drug levels
9/27/93	Telcon w/FDA	Unwitnessed sudden death (120-512-0077) reported, cause UNK; Shaw- call for informational purposes (1st death in AF program) not considered an IND safety report; Chen asked if plasma samples available... yes, but no results available, generally no close correlation has been observed between QT prolongation and plasma levels and data are limited on plasma levels in patient studies.
10/6/93	Submission to FDA	Additional investigators 113, 120; Narrative summary for 120-512
10/13/93	Submission to FDA	Protocol 113B: An Open-Label, Long-Term Extension Study of Orally Administered Dofetilide in Patients With an Implanted Arrhythmia Control Device, first investigator.
10/14/93	Telecon w/FDA	Stein called Roeder: report of unanticipated events in animal safety studies: 2 deaths in 12-mo dog study, req teleconference w/medical reviewer to discuss...scheduled (w/pharmacologist also), Roeder req'd overview of events to be Facsimileed.
10/15/93	Facsimile to FDA	Overview provided by Holmes; conclusion: deaths due to exacerbation of pharmacologic response in individual animals

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10/15/93	Telecon w/FDA	Dog events "serious and unexpected": occurred at dose that should have been well-tolerated based on prev 6mo dog study, subject animals not at the highest dose group, both had highest baseline QTs- may have increased susceptibility, QT prolongations approx 20%, study at 6mo point, noted 200 humans exposed to .5mg BID dose. FDA indicated not overly concerned but req'd clinical safety overview at .5mg BID and below.
10/22/93	Telecon w/FDA	TdP in 4/21 pts in 113, significance unclear- no TdP in UK study 337 (similar pt pop) w/14 pts so far; Tdp may have been related to QT interval excess and pts should have been down-titrated to .25mg BID; narratives offered; EKGs going to consultant for review. FDA req'd a combined overview of 113/337 pt pops instead of narratives, and plasma level info (not available for some time and will be provided once determined).
10/29/93	Submission to FDA	Manufacturing info.
12/2/93	Submission to FDA	Response to FDA request (re: TdP): preclinical toxicology study: full assessment of deaths of two dogs and clinical summary presenting safety and efficacy data, and safety tables provided (reference telecon 10/15/93); requested overview of protocols 113/337 in preparation (reference telecon 10/22/93 with Chen/Roeder).
12/3/93	Submission to FDA	Additional investigators 108B, 113, 113B, 120; Revised FDA-1572s
12/29/93	Submission to FDA	Moller's CV, 002 amendment: mod of diagnostic criteria re liver cirrhosis.
1/12/94	Submission to FDA	Investigator's Brochure (10/93); for 35,009- Additional investigators to protocols 113, 113B, 120; Pouleur's CV; Preclinical report (#93-68-02); Mfg. information
1/18/94	Submission to FDA	Response to FDA request (ref telecon 10/22/93): Cases of TdP in 113 referenced, baseline data listings (drafts) provided for 113/337 (req by Chen), (protocol 109-505 discontinued in mutual agreement with investigator IND 33,984).
1/21/94	Submission to FDA	Amendment to 113: decrease interval between ICD implantation and dosing to accommodate pts with non-thoracotomy leads.
2/11/94	Submission to FDA	Additional investigators to protocol 007-9599, Manufacturing, generic labels.

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3/14/94	Submission to FDA	Pre-clin study report 91-68-81:"Antigenicity Study in Guinea Pigs"; 007-5001 correction; TdP proarrhythmia clarification re: Prot. 113 Pts.
3/16/94	Telecon w/FDA	Pfizer requested EOP II meeting, new CSO assigned to dofetilide.
3/18/94	Telecon w/FDA	EOP II mtg scheduled for 4/21/94
3/18/94	Submission to FDA	115-120 amendment (Canadian HPB request).
3/21/94	Submission to FDA	Annual Report per 21 CFR 312.33
3/29/94	Telecon w/FDA	Notification of discrepancy in listing of expected AEs in IB from previous version; plan for correction.
4/4/94	Telecon w/ FDA	CSO requested status of pre-meeting package, informed of new PK data which would impact discussions at meeting.
4/6/94	Telecon w/FDA	Requested downgrade of meeting based on need to discuss new clinical information.
4/6/94	Submission to FDA	Agenda and pre-meeting package for 4/21/94 meeting.
4/7/94	Telecon w/FDA	Confirmation of time/location for mtg.
4/12/94	Submission to FDA	Additional investigators to protocol (115-113B, -120), Revised FDA-1572s
4/15/94	Submission to FDA	Response to request for information: protocols 115-333, -334, -335 and -336.
4/20/94	Submission to FDA	115-120 amendment: creatine clearance criteria, and exclusion of cimetadine; 115-219 preliminary PK Data; 004 Metabolism Report
4/21/94	Meeting w/FDA	Meeting with Cardio-Renal Division - Discussion of pros and cons of 2nd ICD study. It was proposed to adjust the protocols to assure that individuals with reduced creatinine clearance are not over dosed; Division accepted. Population kinetics plan was also proposed and accepted..
4/25/94	Submission to FDA	115-108B amendment: creatine clearance criteria, and exclusion of cimetadine; 115-219 preliminary PK Data; 004 Metabolism Report.
5/13/94	Submission to FDA	New protocol 115-119: A Randomized, Double-Blind, Parallel, Placebo-Controlled Evaluation of Orally

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		Administered Dofetilide in Patients with Symptomatic Paroxysmal Atrial Fibrillation/Flutter (pAF, pAFL) or Paroxysmal Supraventricular Tachycardia (pSVT), first investigator. 115-113 and 115-113B amendments: creatine clearance criteria, and exclusion of cimetadine. Additional investigator, 115-113B.
5/24/94	Submission to FDA	115-002 amendment: exclusion of women of childbearing potential to meet worldwide program criteria.
6/10/94	Submission to FDA	Additional investigators to protocol 115-113, -113B, -119, Revised FDA-1572s -113, -120.
7/11/94	Submission to FDA	Additional investigators to protocol 115-113, -113B, -119, -120; 1572 mod, IB (V:6/94).
7/21/94	Submission to FDA	Additional investigators to protocol 115-011.
8/3/94	Telecon to FDA	Message to CSO: Pfizer availability for EOP II mtg.
8/3/94	Telecon from FDA	EOP II mtg scheduled.
8/4/94	Telecon from FDA	CSO confirmed date/time of mtg, brief discussion of need for a toxicologist or chemist at EOP II mtg.
8/4/94	Submission to FDA	New protocol 115-005: A Multi-center Pharmacokinetic and Pharmacodynamic Study of Dofetilide in Subjects with stable Atrial Fibrillation (AF) and reduced Left Ventricular Ejection Fraction, first investigator.
8/5/94	Submission to FDA	Additional investigators to protocol 115-113, -113B, -119, -120; 1571 mods, Manufacturing, preclinical .
8/5/94	Submission to FDA	Request for export waiver (dofetilide transdermal patch).
8/24/94	Telelcon to FDA	Discussion of next APR- exclusion of routine safety data from DIAMOND to maintain integrity of blind.
8/25/94	Telecon from FDA	Acceptable to exclude blinded data from 115-400 from the cumulative APR tables.
9/6/94	Telelcon to FDA	Report of case of nodal rhythm in DIAMOND study. Agreed: not 10-day reportable event, continued monitoring for additional events. Written summary req'd by med officer.
9/14/94	Submission to FDA	Additional investigators to protocol 115-113, -113B, -119 and -120; Revised FDA-1572s; CV (P. Dessain);

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		Generic French/English labels, toxicology report (12-mo beagle study).
9/15/94	Telecon to FDA	Discussion of various details related to the EOP 2 meeting (number of desk copies needed, which scientists need to attend, logistics); question raised of running ICD study in Germany under the IND and combining data w/US sites. Also unrelated question: Which CSO to contact for vasodilator compounds for the Tx of male impotence?
9/16/94	Telecon from FDA	Re proposal to combine data from Non-US site with US study data: Dr. Lipicky requested a written proposal.
9/27/94	Telecon from FDA	Change of EOP 2 mtg time, request for status of pre-meeting information package.
9/27/94	Submission to FDA	Re EOP 2 meeting: confirmation of mtg, Pfizer mtg minutes for the 4 previous mtgs (1/90, 4/92, 4/93, 4/94), information package, proposed agenda, participants list.
10/5/94	Telecon to FDA	Left message: requested confirmation that tox and chemistry representation not needed for EOP 2 mtg.
10/6/94	Telecon from FDA	Pharmacology and Chemistry reviewers will be at meeting but have no issues to discuss, Pfizer representation not needed.
10/7/94	Submission to FDA	Request for Division's minutes from 4/21/94 meeting.
10/7/94	Submission to FDA	Additional investigators: 115-002, -005, -113, -113B, -119, -120; tox report.
10/17/94	Submission to FDA	EOP 2 mtg details, revised draft labeling, final agenda and participants list.
10/31/94	Corresp. from FDA	FDA-prepared minutes from 4/21/94 meeting.
11/3/94	Submission to FDA	New Protocol 115-120X: "Effects of Conversion to Sinus Rhythm on Exercise Tolerance in Patients with Chronic Atrial Fibrillation: A Substudy of the (...115-120...)", first investigator.
11/4/94	Telecon to FDA	Initial inquiry re: deletion of certain CRF data items not pertinent to the evaluation of safety and efficacy. CSO will communicate question to medical reviewer, additional information will probably be required.
11/10/94	Telecon from FDA	Medical reviewer called re: 115-120X; requested information on inclusion of proarrhythmic nature of

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		exercise testing in IB and ICF for 115-120X; provided current texts via return voice-mail; return comments requested by Pfizer.
11/10/94	Submission to FDA	Additional investigators to protocol 113, 113B, 119, 120, 1572 modifications.
11/16/94	FDA Log	Pfizer-prepared minutes from the 10/20/94 EOP-2 meeting.
11/16/94	Submission to FDA	New Protocol 115-120A: "A Double-Blind Long-Term Extension Study of Orally Administered Dofetilide in Patients Having Previously Completed the Dofetilide Study 115-120: <115-120 title>", first investigator.
11/17/94	Telecon from FDA	Medical Reviewer requested stronger wording of risks in 115-120X ICF and revision to IB. Agreed to IB revision in post-annual report update.
11/22/94	Submission to FDA	Additional investigators to protocol 119, 115-120, 1572 modification.
11/23/94	Submission to FDA	Pfizer prepared minutes of the 10/20/94 EOP-2 meeting, FDA-prepared meeting minutes requested.
12/6/94	Telecon and Facsimile to FDA	Informed Medical Reviewer that requested changes made to 115-120X ICF, protocol also amended; amended pages facsimiled for reviewer's approval; also confirmed IB revision will follow the AR and current IB may be used until update is available.
12/7/94	Telecon from FDA	Medical Reviewer reviewed revised 115-120X protocol and ICF, agreed with changes.
12/22/94	Submission to FDA	Protocol amendment: 115-120X (as discussed in 12/6-7/94 logs).
1/9/95	Corresp. from FDA	FDA-prepared minutes from the 10/20/94 EOP-2 meeting with the Division.
1/9/95	Telecon to FDA	Request for meeting with medical reviewer to discuss proposed CRF line listing deletions (ref entry 11/4/94) and information required for reviewer to evaluate request.
1/11/95	Meeting w/FDA	Discussion of 13 items proposed for omission from the CFRF line listings; outcome: 5 items out, 6 items stay, 2 need more info for decision by med. reviewer. Reviewer requested Pfizer use a specific format for protocol information.

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1/13/95	Facsimile from FDA	Above-mentioned "format" Facsimiled, expected format to pertain to CFRF line listings, but Facsimile titled "data presentation sheet."
1/17/95	Telecon to FDA	Clarification on the data presentation sheet: it is an example of how the Division would like protocol information summarized, the medical reviewer is available to work with Pfizer on the design of the tables for the dofetilide NDA.
1/30/95	Submission to FDA	Additional investigators to protocol 115-113, -113B, -119, -120, -120A, Manufacturing.
1/31/95	Telecon w/FDA	Request for meeting to discuss minimal reporting format for certain studies, reporting of the DIAMOND sub-studies, continuation of discussion on the CRF tabulation line listings; CSO indicated a meeting may not be necessary and requested a pre-meeting package for review.
2/3/95	FDA log	Discrepancies noted between the Division and Pfizer meeting minutes, log lists eight clarifications to FDA meeting minutes.
2/8/95	Submission to FDA	Clarification of discrepancies in FDA-prepared meeting minutes (ref. 2/3/95) sent to the Division.
2/9/95	Submission to FDA	Pfizer-prepared minutes from 1/1/95 meeting with Medical Reviewer (discussed CRF tabulation line listings).
2/20/95	Submission to FDA	Additional investigators to protocol 113, 113B, 119, 120, 120A, 120X; 1572 modifications; manufacturing.
2/20/95	Submission to FDA	Holter tape w/TdP, as requested by Dr. Lipicky for "scientific interest."
2/22/95	Submission to FDA	Annual report.
2/23/95	Submission to FDA	Amended protocol 120X
3/8/95	Telecon with FDA	Case report form tabulations discussed; request for 10 grams "research grade" dofetilide for Dr. Lipicky
3/23/95	Facsimile from FDA	Request from Dr Lipicky for 10g dofetilide and CP-101606 to study effects on ionic conductances of squid giant axon at marine biological laboratory
3/28/95	Submission to FDA	Additional investigators to protocol 113-670, 113B-605, 119-676; Mods 002-565, 108B-502

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4/11/95	Submission to FDA	Additional investigators to protocol 108B/113/113B/191/120X; Mods 119-679, 120-568; Sudden Unexpected Cardiac Deaths (SUCD) report
4/3,6,12,17/95	Telecons to FDA	Questions re usefulness of data for regulatory purposes from protocol 117; request for meeting to discuss DIAMOND studies
4/25/95	Submission to FDA	Information Package Re Diamond Studies For Chen
5/5/95	FDA Meeting	Discussion re protocol 115-117; NDA
5/15/95	Submission to FDA	Additional investigators to protocol 113/113B/117/119/120A/120X; Sudden Unexpected Cardiac Deaths (SUCD) Report; manufacturing
5/17/95	Telecon with FDA	Submitting non-clinical data (CMC, pharmacology, toxicology) to the IND prior to the NDA
5/18/95	Submission to FDA	05-May-95 Meeting Minutes
5/24/95	Submission to FDA	Request copy of FDA Meeting Minutes
6/1/95	Letter from FDA	05-May-95 FDA Meeting Minutes
6/5/95	Submission to FDA	Preclinical
6/6/95	Facsimile from FDA	09-Apr-93 Meeting Minutes
6/7/95	FDA Log	Received minutes form 5/5/95 & 4/9/93 meetings
6/15/95	Submission to FDA	Additional investigators to protocol 120,120X; Revised FDA-1572s
7/20/95	Submission to FDA	Additional investigators to protocol 108B,113B,119, 120A; Revised FDA-1572s; Bonney's CV; Preclinical
7/28/95	Submission to FDA	New protocol 115-119A: - A Double-Blind Long-Term Extension Study of Orally Administered Dofetilide in Patients Having Previously Completed the Dofetilide Study #115-119: A Randomized Double-Blind Parallel Placebo-Controlled Evaluation or Orally Administered Dofetilide in Patients with Symptomatic Paroxysmal Atrial Fibrillation/Flutter (pF, pAFL) or Paroxysmal Supraventricular Tachycardia (pSVT); Additional investigator 119A-637
08/01&02/95	Telecons	Interim analysis for 115-119 can not be completed and merged with main database before AR filing date; request to submit safety data for this study separately in the AR. This was accepted.

DATE	ACTIVITY	COMMENTS
		Emergency Use IND: Chen suggested to modify an existing open label protocol with a broad enough amendment to make dofetilide available on an emergency use basis.
08/04/95	Submission to FDA	Emergency Use Letter of Authorization
08/08/95	Submission to FDA	Safety Report: Australian patient with mild angioedema 3455-232-0509; Dear Doctor Letter; ICF Addendum
08/28/95	Submission to FDA	IB (Aug-95)
09/12/95	Submission to FDA	Additional investigator to protocol 113B; Revised FDA-1572s; Preclinical ; SUCD report
09/20/95	Telecon	Request for Holter tape with self-timing TdP first made at EOP2 Mtg. 10/20/94. After submission and review of such tape, issue of polymorphic VT vs. TdP arose and additional Holter tapes were requested to demonstrate arrhythmia due to drug-induced TdP as well as example of polymorphic VT. Mtg. set for 12/1/95 to review.
09/26/95	Submission to FDA	Protocol 108B Modification
10/05/95	Submission to FDA	Additional investigator to protocols 113,113B,119,119A,120X; Revised FDA-1572s; Preclinical
11/02/95	Submission to FDA	Additional investigators to protocols 108B/113B,120A; Revised FDA-1572s
11/9,13,14/95	Telecons with FDA	Negotiations over meeting date and Holter reader availability; Holter tape review meeting had to be rescheduled to January per Lipicky's request due to Medifact's move. E-sub demo meeting date established.
12/05/95	Submission to FDA	Additional investigators to protocols 113B,119.119A
12/15/95	Telecon with FDA	Copies of 4 Holter Tapes sent to Div. for 1/10/96 Mtg.
12/18/95	Submission to FDA	Holter Tapes, Participants For 10-Jan-96 Meeting
01/05/96	Submission to FDA	Additional investigators to protocols 108B,119A,120A
01/29/96	Submission to FDA	New Protocol 254 - An Open Randomized Three-Way Crossover Study to Compare the Bioavailability of Dofetilide When Given as 1) Commercial Capsule With

DATE	ACTIVITY	COMMENTS
		Cross Linked Gelatin Shell 2) Commercial Capsule With Non-Standard Dissolution Profile and Commercial Capsule With a Standard Dissolution Profile; Purkins Cv
02/08/96	Submission to FDA	New Protocol 128 - A Randomized Double-Blind Parallel Placebo-Controlled Evaluation of Orally Administered Dofetilide in Subjects With Symptomatic Paroxysmal Atrial Fibrillation or Flutter (pAF Or pAFL); Manufacturing
02/23,26,28/96	Telecons with FDA	Request by Chen to have secondary efficacy analysis performed which includes recurrence of AF/AFl during first 3 days of dofetilide administration. Agreement to add this analysis to the protocol
03/05/96	Submission to FDA	Additional investigators to protocols 119A,120A,128; Revised FDA-1572s
03/05/96	Meeting with FDA	Lipicky requests examples of TdP Holter Tapes. Issue: distinguishing TdPs from PMVTs
03/08/96	Submission to FDA	Response: Protocol 128 CRFS Requested By Dr. Chen
03/13/96	Submission to FDA	Revised FDA-1572; SUCD Report
03/22/96	Submission to FDA	New Protocols 012 - An Open-Label Crossover Study to Determine the Bioequivalence of a Proposed 0.5 mg Commercial Capsule of Dofetilide Relative to the 0.5 mg Research Capsule in Healthy Male or Female Subjects; New Protocol 014 - An Open-Label Crossover Study to Determine the Bioequivalence of Two 0.5 mg Research Capsule Formulations of Dofetilide in Healthy Male or Female Subjects; Gardner's CV
04/02/96	Telecon with FDA	Stockbridge suggested Pfizer request a waiver from providing CRF line listings in the NDA
04/02/96	Submission to FDA	Additional investigators to protocols 108B,128; Revised FDA-1572s
04/10/96	Submission to FDA	Annual Report (Aug-95)
04/19/96	Submission to FDA	Electronic Demonstration At SAS Institute: Schedule And Pfizer Attendees
04/24/96	Meeting at SAS Institute	E-Sub Demonstration
05/10/96	Submission to FDA	Additional investigators to protocols 005,119A,128; Revised FDA-1572s

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05/29/96	Submission to FDA	Additional investigators to protocols 119A,128
06/06/96	Letter from FDA/telecon	EOP2 Meeting Preparations; CMC Info from Zimmerman
06/18,20/96	Telecons	Parekh questioning the necessity to perform 012 and suggested waiver under the SUPAC
06/26/96	Submission to FDA	Additional investigators to protocols 119A,120A,128; Revised FDA-1572; Preclinical ; SUCD report
07/10/96	Facsmile from FDA	CMC and Biopharm Queries From Review of Submission
08/21/96	Submission to FDA	DIAMOND Statistical Analysis Plan; Confirmation/Agenda of 9/27/96 Meeting
08/22/96	Submission to FDA	Response to FDA queries from 7/10/96 regarding two bioequivalence studies 115-012 & 115-014: 1. Formulations and lot sizes for research & commercial dosage forms; 2. Active metabolites; 3. 48 hr sampling covering 3-4 T1/ 4. Assay validation data; 5. Evaluation of bioequivalence
08/29/96	Submission to FDA	21 CFR 312.30 New Investigators to protocol 119A, 120A, 128; 1572 Form Modifications
09/06/96	Submission to FDA	AF meta-analysis proposal for the DIAMOND trial (by Pritchett & Wilkinson) for 9/27/96 meeting
09/06/96	Fax from FDA	ICH Draft Guidelines on the Impurities in New Drug Substance (from Zimmerman)
09/24/96	Submission to FDA	21 CFR 312.30 and 312.31Additional Investigators to protocol 119A, 128; 1572 Form Modifications; SUCD Quarterly Report
09/24/96	Submission to FDA	re: 9/27/96 Meeting to discuss DIMOND Statistical Analysis Plan; submitting current version & subsequent amendments to Protocol 400
10/25/96	Submission to FDA	21 CFR 312.30 Principal Investigators to protocol 119A and 128; 1572 Form Modifications
10/29/96	Submission to FDA	Pre-Meeting materials for 11/20/96 EOP2/CMC Mtg; Slides and Summary Document
11/05/96	Submission to FDA	9/27/96 Meeting Minutes re: DIAMOND Statistical Plan
11/15/96	Submission to FDA	Response: Rationale for Bioequivalence study 012/013
11/19/96	Letter from FDA	FDA prepared meeting minutes from the 9/27/96 meeting re: DIAMOND Statistical Plan

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12/02/96	Submission to FDA	New Protocol 115-015: An Open-Label, Crossover Study to Determine the Effect of Food on the Pharmacokinetics of Dofetilide when Administered as a 500µg Commercial Capsule; Protocol Amendment to 115-012; Revised 1572 Form
12/06/96	Submission to FDA	Manufacturing Information
12/09/96	Submission to FDA	New Protocol 115-013: An Open-Label, Crossover Study to Determine the Effect Bioequivalence of a 125µg Commercial Capsule of Dofetilide, Relative to the 500µg Research Capsule , in Healthy Male or Female Subjects
12/11/96	Submission to FDA	11/20/96 End of Phase II CMC Meeting Minutes; Request for Division Minutes
12/12/96	Submission to FDA	Revised Annual Report (Mar '96)
12/16/96	Submission to FDA	Revised FDA 1572 Forms; Manufacturing Information
12/18/96	Submission to FDA	New Investigator, 115-005; Manufacturing Information; SUCD Quarterly Report
01/03/97	Submission to FDA	Annual Report (8/18/95 - 9/20/96)
01/06/97	Submission to FDA	New Protocol: A Randomized, Double-Blind, Parallel, Placebo-Controlled Evaluation of Orally Administered Dofetilide in Subjects with Symptomatic Paroxysmal Atrial Fibrillation or Flutter (pAF or pAFL); New Investigator
01/08/97	Submission to FDA	Proposal for Tradename of Xelide
01/03,07,10/97	Telecons with FDA	Agreement that SUCDs need not be reported on a quarterly basis; Staged NDA should be submitted within 120 day period as specified in the regulations
01/31/97	Submission to FDA	Criteria lists which distinguish between protocol violations and protocol deviations (Request from 9/27/96 Mtg.)
02/04/97	Telecon with FDA	Obtaining Division agreement on staged submission of the Dofetilide NDA and that initial filing would not include a complete CMC section; Received FDA minutes for 11/20/96 EOP2 CMC Mtg.
02/07/97	Submission to FDA	Additional Investigators to protocol 128A; Revised FDA 1572 Forms; Manufacturing Information; Preclinical Information
02/26/97	Submission to FDA	Additional Investigators to protocol 128A
04/07/97	Submission to FDA	Pre-NDA Mtg Package per 21 CFR 312.47 for 4/23/97 Mtg.

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04/08,11,16,18,21/97	Telecons with FDA	Request by Pharmacology Reviewer (Gill-Kumar) for additional information re: carcinogenicity studies
04/28/97	Letter from FDA	Questions by Chemistry Reviewer (Zimmerman) on CMC submission
05/23/97	Submission to FDA	Amendment to Protocol 120A; New Investigator to Protocol 119A; Revised FDA 1572 Forms
05/23/97	Fax from FDA	Biopharm NDA Wish List
05/28/97	Telecon with FDA	Agreement to have Biopharm data provided as part of the E-sub for all relevant Biopharm studies
06/23/97	Submission to FDA	Revised FDA 1572 Forms and Pre-NDA Meeting Minutes from 4/23/97
06/30/97	Corr. from FDA	Summary of Pre-NDA Meeting 4/23/97
07/14/97	Submission to FDA	Response to FDA request for information regarding preclinical reports (dose selection/tumor types)
07/18/97	Submission to FDA	Pre-NDA Meeting Information for 8/8/97 per 21 CFR 312.47
07/9,11,16,18/97	Telecons with FDA	CMC Mtg. confirmed; Mtg. Pkg. at FDA on 7/21/97;extra copy of safety study to pharmacology reviewer
07/25/97	Submission to FDA	Updated Investigator's Brochure (5/97); Additional Investigator to protocol 542; Revised FDA 1572 Form
07/29/97	Submission to FDA	Response to FDA request for information on Carcinogenicity studies for Group B Data Set
07/30/97	Fax from FDA	Comments by FDA Chemistry Reviewer (Zimmerman) on pre-meeting package for 2nd CMC pre-NDA Mtg 8/8/97 (re: blister packs)
08/06/97	Fax from FDA	Inspectional Information and related topics for FDA/CMC Meeting 8/8/97 (from Zimmerman)
08/11/97	Telecon with FDA	Lipicky agrees to 7/28/97 meeting to discuss results of the DIAMOND trial
08/26/97	FDA Log	Meeting minutes from 8/8/97 (re: Dissolution tests, Stability Program, OOS Results, Chromatographic tests, Starting Material)
08/26/97	FDA Log	Meeting minutes from 7/28/97 (re: DIAMOND CHF trial results)

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09/25/97	FDA Log	Discussion between Lipicky & Friedrich (at Berlin symposium) re: 115-113; Dosage; AF studies pooled survival analysis; Filing date(s)
10/7,10/97	Telecons with FDA	Request for NDA number
10/13/97	Submission to FDA	Proposed Tradenames: Restosyn, Tikosyn, Allsync, Enablex
10/23/97	Submission to FDA	Revised FDA 1572 Forms; Meeting Minutes from 8/8/97
11/14/97	Letter from FDA	FDA Meeting minutes from 8/8/97 Pre-NDA Meeting
11/5,12,14,17/97	Telecons with FDA	E-sub orientation scheduled for 11/25/97; NDA submission I date set for 11/25/97; computer upgrades for reviewers; summary of all studies in Dofetilide clinical program for Gordan.

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11/25/97	Submission to FDA	Initial NDA Submission
12/05/97	Letter from FDA	Acknowledge receipt of pre-submission of certain chemistry and partial information for NDA 20,931
12/12/97	Telecon with FDA	Assignment of User Fee ID #3390
01/12/98	Fax from FDA	Tips from Zimmerman submitting helpful NDA (rolling) information with next stage for drug product
01/26/98	FDA Log	Telecons with FDA: Clarification on two DIAMOND arrhythmia tables; Summary listing of all Dofetilide Clinical studies; Discussion of secure e-mail link; Electronic filing of archival version of CRFs and CRF tabulations
03/04/98	Letter to FDA	NDA Transfer Notification
03/04/98	Letter to FDA	PPPCL Confirmation of NDA Transfer
03/6,11,12/98	Telecons with FDA	Proposal for guidance compliant archive tape for the dofetilide NDA; technical issues with electronic archiving resolved.
03/03,06,09,16/98	Telecons with FDA	Selection of Statistical Reviewer for the dofetilide NDA; selection of additional Medical Reviewers; computer issues
03/09/98	Submission to FDA	Initial NDA Submission Additional Volumes
03/16/98	Letter from FDA	Assigning NDA 20,931
03/19/98	Letter from FDA	Acknowledge receipt of transfer of ownership to PPPCL 3/4/98

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03/19,23,27	Telecons with FDA	Information requested (Burnett) for DSI inspection of investigator sites: NDA TOC, protocols, blank CRFs, and monitoring SOPS
03/24/98	Letter from FDA	
03/26 & 4/6/98	Telecons with FDA	re: Transfer of NDA to new sponsor; letters of transfer sent 3/4/98; new form 356h required because NDA transfer separate from NDA filing
03/24/98	FDA Log	re: "P" review; internal FDA meeting among reviewers to reach final decision on 4/14/98 (Until that date, reviewers instructed to work on the NDA as a "P" review)
03/24,31/98	Telecons with FDA	re: revised Debarment statement (omitting "to the best of its knowledge" phrase)
04/01/98	FDA Log	re: telecons 2/19,23,25,27 & FDA Pre-NDA Meeting Minutes - Parekh agrees that BE study not required as long as appropriate BE study linkages are included in the NDA
04/02/98	Fax from FDA	Request for clarification re: summary of safety - actual dose received analysis
04/06/98	Fax from FDA	Request for description of drop out category "other" of Table H.6.2.10 discontinuation from treatment
04/08/98	Submission to FDA	Revised debarment statement
04/09/98	Submission to FDA	New Form FDA 356H
04/10/98	Submission to FDA	Data for the Division of Scientific Investigations
04/15/98	FDA Log	re: telecons 3/21 & 4/6,8,9 - Plans for meeting to discuss QT prolongation issues
04/16/98	Fax from FDA	Request for information Tables H6.21.2 and H.6.19.2
04/20/98	Fax to FDA	Response to Ganley's request (4/15/98) for list of submission dates of initial protocols
04/22/98	Fax from FDA	Summary of treatment emergent adverse events
04/28/98	Letter to FDA	Appeal of the standard review
04/28/98	Fax from FDA	Zimmerman CMC concerns about ICH validation of photo-stability methods
04/29/98	FDA Log	Telecon with FDA 4/16 - Request by Gill-Kumar for reference list assistance; response faxed to FDA 4/24
04/30/98	Submission to FDA	Desk copies as requested by Drs. Ganley & Cui

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04/30/98	Fax from FDA	Zimmerman stability review comments and requests
05/04/98	Fax from FDA	Zimmerman comments about non-compendial excipient controls - inks and colorants
05/05/98	FDA Log	Ganley request re: Conduct of study 120; EKGs for 120 and 345
05/05/98	Letter to FDA	re: Gordon request (4/6/98 fax) - "Other" patient dropouts; Discrepancy in QT/QTc intervals in two ASV tables
05/05/98	Fax from FDA	Methods validation comments about sample selection
05/08/98	Submission to FDA	CMC Photostability (Response to Zimmerman query)
05/11/98	Fax from FDA	"To be approved" stability protocol considerations (Zimmerman)
05/12/98	Fax from FDA	Child resistance packaging issues for blisters; reference to PPPA concerns
05/13/98	Submission to FDA	Proposal for new safety summaries; response to Gordon 4/22/98 fax query
05/15/98	Submission to FDA	Five responses to queries
05/15/98	Submission to FDA	Protocol modifications to 108B, 113B, 119A, 120A, 128A; Revised FDA 1572 Forms; Manufacturing Information
05/17/98	Fax from FDA	Gordon's request for identity of patient and dose of drug
05/19/98	Telecon from FDA	Queries from Statistical Reviewer: DIAMOND efficacy data; Population PK/PD NONMEM analysis; In vitro dissolution data
05/20/98	Submission to FDA	Response to Zimmerman query re: CMC/Mfg.
05/22/98	Fax to FDA	Efficacy datasets for study 400 AF; Safety Summary Proposal
05/22/98	Submission to FDA	Response regarding 120 EKGs
05/28/98	Fax to FDA	Response to Fadiran regarding individual in vitro dissolution data
05/28/98	Fax to FDA	Response to Zimmerman re: 5/11 & 12 queries on stability protocol considerations and Blister Pack child resistance issues
05/29/98	Fax to FDA	Errata and updates to the CMC and MV sections to the NDA

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06/03/98	Submission to FDA	Response to Zimmerman queries regarding CMC
06/03/98	Fax from FDA	Request for number of patients in each age category of adverse events reports summary (Gordon)
06/05/98	Fax from FDA	Temple's reasoning behind decision to deny priority review
06/09/98	Fax to FDA	Response to Cui providing the interim efficacy results for the primary and five defined secondary efficacy endpoints in DIAMOND CHF and MI
06/09/98	Submission to FDA	Safety Update
06/11/98	Fax from FDA	FDA/CMC Evaluative information provided to Pfizer NDA 20,931
06/11/98	Telecon with FDA	Request for EKGs for TdP cases (Gordon)
06/12/98	Fax to FDA	Response to query (Gordon 6/3/98)
06/16/98	Submission to FDA	Response to statistical queries (Williams 5/14 & 21) re: DIAMOND 115-400CHF/MI
06/16/98	Fax from FDA	Request for further information on potential drug interaction effects (Gordon)
06/22/98	Submission to FDA	Response to query (Gordon 6/3 & 4) providing serious adverse event summary tables by age and gender
06/24/98	Fax from FDA	Request for information for evaluation of drug-drug interaction studies (Gordon)
06/24/98	Fax from FDA	Minutes of a telecon between Pfizer and the FDA
06/25/98	Submission to FDA	Response to queries by Cui, Fadiran, Gill-Kumar and Resnick
06/29/98	FDA Log	re: telecons with FDA - CAC recommendation for steady state PK study in rats and mice
07/01/98	Telecon with FDA	Request for datasets for two studies (Fadiran)
07/01/98	Submission to FDA	Response to query (Ganley 4/22 & 24) regarding 345 ECGs
07/02/98	Fax from FDA	Request for clarification on ISS Section H.6.C (Gordon)
07/02/98	Telecon with FDA	Request for information by Ganley about disposition of subjects in Table 6.1 (Conversion to Sinus Rhythm table); Table 4.1 (Discontinuation table); Table 5 (Maintenance Period)

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07/10/98	Submission to FDA	Response to request for safety analysis by actual dose (Gordon)
07/13/98	Telecon with FDA	Addressing concern by Ganley about the reliability of the Danish registry system which provides follow up information on patients in the DIAMOND trials.
07/14/98	FDA Log	re: telecons with FDA: 6/8, 15, 16, 24, 25 & 7/1 & 10 - Previously scheduled meeting to discuss collaboration on examining the relationship between QTc and mortality postponed until proposal finalized
07/14/98	Telecon with FDA	Agreement of two European sites to be inspected by Division of Scientific Investigations Sept/Oct '98
07/16/98	FDA Log	re: telecons with FDA: 6/25, 7/1, 7, 10, 14 - Follow-up on query about statistical analysis of the DIAMOND datasets
07/21/98	Submission to FDA	Reformatted SAS Datasets/Response to (Williams) Statistical query
07/21/98	Fax to FDA	Response to 7/2/98 query (Gordon) - information on premature discontinuations (Sec. H.6.C)
07/24/98	Submission to FDA	Response to Ganley request (telecons 7/1, 2 & 14) re: discontinuations; submitted splits of tables 4.1 & 4.2
07/27/98	Fax to FDA	Response to request for concurrent medications summary table for study 115-400CHF (Williams)
07/28/98	Submission to FDA	Response to 7/20/98 query (Gordon) requesting information on premature discontinuations; also, concomitant medications summary table
07/31/98	Submission to FDA	Response to Fadiran: In vitro data sheets from drug metabolism studies
08/03/98	Fax from FDA	Request for denominators for the 3 deaths shown in the table from the ISS (Gordon)
08/07/98	FDA Log	re: telecons with FDA 7/24, 28, 8/4 & 5 - Pre-Advisory Committee meeting scheduled for Sept. 16, 1998
08/07/98	Submission to FDA	Response to query (Parekh) providing P-GP interaction data
08/14/98	Fax from FDA	Statisticians request (Cui) associated with the hypothesis testing scheme specified in the protocol of the DIAMOND trial
08/18/98	Submission to FDA	Response re: Meeting between Williams/Cui/Hilton discussing DIAMOND issues

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08/20/98	Submission to FDA	Response to queries (Gordon & Williams 6/24, 7/29 & 8/3/98)
08/20/98	FDA Visit (Cui)	Datasets installed on FDA esub server
08/22/98	Fax from FDA	Draft of the Gender Section of Safety Review & Request for explanation of why the dose of the OC was given 2 hrs. after the dose of dofetilide in 115-236 (Gordon)
08/24/98	Fax from FDA	Request (Gordon)for means for the QTc Intervals in Table 6.3.1 (115-001)
08/24/98	Fax from FD	Request (Gordon) for the mean QTc Intervals for Table 6.3 (115-004)
08/24/98	Fax to FDA	Final response to request for additional information regarding DIAMOND 115-400
08/28/98	Fax from FDA	19 Questions regarding 115-345 (Ganley)
08/28/98	Fax from FDA	Sample Form Letter (DSI)
08/31/98	Fax to FDA	Response to request (Gordon) for the mean QTc intervals for Table 6.3.1 for 115-001/004
08/31/98	FDA Log	re: 8/20/98 Mtg. Summary discussing Cytochrome P450 3A4 Inhibitor-Dofetilide drug interaction study and PK/PD issues
09/02/98	Submission to FDA	Response to request for information regarding QTc Intervals and design of 115-236
09/03/98	Fax from FDA	FDA Minutes of 5/14/98 telecon (Williams/Cui & Pfizer) re: DIAMOND study
09/03/98	Fax from FDA	Request for information regarding data on the reproductive toxicology studies (Gill-Kumar)
09/08/98	Fax from FDA	Request for information regarding 115-120 & 115-345 (Ganley)
09/08/98	Telecon with FDA	Discussing his queries regarding efficacy data by gender for 120 & 345 with Ganley
09/09/98	Submission to FDA	Response to request for publications (Gill-Kumar)
09/10/98	Fax to FDA	Response to questions regarding 115-120 and 115-345 (Ganley 9/8/98)
09/10/98	Fax to FDA	Additional information re: Gwilt publication; also, response to toxicology query
09/10/98	FDA Log	re: telecons 9/1, 4, 8, 9 with FDA - Negotiations for

DATE	ACTIVITY	COMMENTS
		September 11, 1998 meeting; draft AC briefing document
09/11/98	Letter from FDA	FDA Meeting Minutes of 8/20/98 meeting between FDA & Pfizer
09/11/98	Submission to FDA	Draft dofetilide - hormone replacement therapy interaction protocol 115-116
09/11/98	Fax to FDA	Response to DIAMOND statistical queries (Cui/8/14/98)
09/16/98	Mtg. with FDA	Pre-Advisory Committee Meeting
09/18/98	Telecon with FDA	Request for 90% confidence intervals for plasma level data for males and females for 115-016 (Fadiran)
09/18/98	Telecon with FDA	Request for assistance to locate tables in DIAMOND summary report (Chen)
09/18/98	Telecon with FDA	Request for Ketoconazole interactions protocol
09/21/98	Fax from FDA	Request for information regarding 115-372 (Ganley)
09/22/98	Fax to FDA	Providing a copy of 115-311 (to Ganley)
09/23/98	FDA Log	Summary of Pre-Advisory Committee Meeting 9/16/98 (ACBD - Lipicky emphasis on efficacy - Increased risk of TdP in women)
09/25/98	Submission to FDA	re: Meetings with Division 8/20, 9/11 & 9/16 regarding documents reviewed and discussed; submitting these documents to the FDA files.
09/28/98	Submission to FDA	Responses (and modification to previously submitted response) to Cui, Gill-Kumar, Ganley and Burnett queries
10/01/98	Fax from FDA	Questions regarding glucose bicarbonate or lipid profiles in the NDA (Gordon)
10/02/98	FDA Log	re: telecons 9/28, 29, 30, 10/1 with Cui Request for S-Plus
10/02/98	Fax from FDA	Request for information regarding 115-345, -120 & -119 (Ganley)
10/05/98	Fax to FDA	Providing information regarding request (by Burnett) for number of patients randomized at each 115-119 study site
10/07/98	Fax from FDA	Request for information regarding 115-119 (Ganley)
10/07/98	Fax from FDA	Request for information regarding drug substance, drug product, and labeling issues (Zimmerman)

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10/07/98	Fax from FDA	Zimmerman slides regarding Innerseal discussed with Hollander (telecons 8/14, 18, 24 & 10/1, 7)
10/09/98	Submission to FDA	Updated information (4 enclosures)
10/09/98	Submission to FDA	Providing information regarding issues discussed in telecons 7/24, 27 & 30 (with Fadiran & Parekh)
10/13/98	Submission to FDA	Providing additional CMC information (re: 4/30/98 Zimmerman request) and 115-254 Dissolution data (re: 9/28/98 Fadiran request)
10/16/98	Submission to FDA	Response to faxed queries (9/21/98 & 10/2/98 Ganley) regarding 115-372 & 115-119
10/16/98	Fax from FDA	Draft medical/statistical review: efficacy data (from Ganley)
10/19/98	Fax from FDA	Request for Investigator-identified proarrhythmic events that did not meet the protocol definition including treatment group and reason for exclusion from ISS (Gordon)
10/19/98	Fax from FDA	FDA Meeting Minutes of 9/16/98 Pre-Advisory Committee Mtg
10/19/98	Submission to FDA	Responses to requests (Ganley 8/28, 9/8, 10/2) regarding studies 115-345/120/119
10/22/98	Fax from FDA	Request for information regarding 115-128 and 115-363 (Ganley)
10/27/98	Submission to FDA	Response to query (Zimmerman 10/7/98) regarding drug substance and drug product
10/28/98	Submission to FDA	New Protocol (Draft):"A parallel, Single-Blind Study to Determine the Effect of Hormone Replacement Therapy, and Gender, on Dofetilide Pharmacokinetics Additional Investigator 016-5007
10/28/98	Corresp. from FDA	FDA Minutes of Teleconference 10/7/98
10/29/98	Submission to FDA	Response to faxed queries (10/1/98 and 10/19/98 Gordon)
11/04/98	Fax to FDA	Draft Safety Overview from T. Friedrich to M. Gordon
11/05/98	Corresp. from FDA	Comments from 3/9/98 submission
11/05/98	Corresp. from FDA	Comments from 3/9/98 submission (safety review)
11/06/98	Submission to FDA	Response to teleconferences (9/28 & 10/20) and to Meeting (8/20/98) regarding 115-254 and 115-239

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11/12/98	Submission to FDA	Response to faxed query (4/30/98 Zimmerman) requesting additional stability information
11/12/98	Corresp. from FDA	Comments from 3/9/98 submission
11/13/98	Submission to FDA	Response to teleconferences (11/3 & 11/5/98 Cui & Andrews)
11/17/98	Submission to FDA	Response to Fax (10/22 Ganley), telecon (8/24 Gordon), telecon (6/25 Williams) and conversation with Lipicky (10/22/98)
11/17/98	FDA Log	FAX from Mr. Roeder with Dr. Cui's statistical review of the DIAMOND studies (attached).
11/17/98	FAX to FDA	Sent to Dr. Ganley with response to request for patient status (draft).
11/17/98	FAX to FDA	Sent to Dr. Zimmerman water content and water absorption data requested (attached)
11/17/98	FAX to FDA	4th interim results sent to Dr. Cui.
11/17/98	FAX from FDA	Statistician questions.
11/19/98	FAX to FDA	Sent to Mr. Roeder to be given to Dr. Gordon for discussion with Dr. Friedrich.
11/19/98	FAX to FDA	Sent to Dr. A. Williams: additional info on DIAMOND AF sub-study and mortality curve.
11/20/98	FDA Submission	re: response to FDA request for information. Enclosure 1: additional info o 115-119. Enclosure 2: additional info on 115-363. Enclosure 3: final response to question regarding final status of patient 115-365-419-0209. Enclosure 4: additional info regarding first assay for study 115-254.
11/20/98	FAX to FDA	Sent to Dr. A. Williams: Kaplan-Meier graph for dofetilide/placebo comparison.
11/23/98	FDA submission	CMC amendment.
11/23/98	FDA Log	Meeting with Division. Nov. 17, 1999: Discuss Dr. A. Williams' review of DIAMOND AF sub-studies. FAX sent with graph and comparison. Nov. 19, 1999: Requested telecon to discuss FAX. FAX discussed.
11/23/98	Telecons with FDA	Nov. 13, 1998: With Mr. Roeder to discuss plans for Nov. 23 meeting to discuss briefing document. Nov. 17, 1998: Request to call Dr. Gordon. Discussed briefing document. Nov. 18, 1998: Request to speak with Dr. Lipicky. Nov. 19,

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		1998: FAX to Mr. Roeder re: Dr. Gordon's safety review (to serve as basis of discussion for Drs. Friedrich and Gordon).
11/24/98	FDA submission	re: CMC update. Four desk copies to Mr. Roeder.
11/24/98	FDA Submission	Protocol amendment, change in protocol and Information amendment, pharmacology/toxicology. Final protocols submitted. Enclosure 1: Standard Protocol No. 048. Enclosure 2: Standard Protocol 026. Enclosure 3: Protocol. 115-016 is currently being amended.
11/24/98	Telecon with FDA	11/20/98: Ms. Standaert and Dr. Murphy to discuss AC issues.
11/24/98	FDA Log	Meeting with Dr. Gordon, Dr. Murphy and Mr. Andrews to discuss various aspects of Dr. Gordon's safety review.
11/24/98	FAX to FDA	Sent to Dr. Lipicky. Final response to question re: number of symptomatic cases of TdP and which were identified through Holters (draft response sent Nov. 9, 1998).
11/25/98	FDA submission	Re: response to FDA request for information. Response to question around TdP cases and Holter monitoring. Desk copy to Dr. Lipicky.
11/25/98	FAX to FDA	Draft of info requested by Dr. Gordon sent to same (revision of table in Dr. Gordon's Safety Review).
12/01/98	Telecon with FDA	Dr. Fadiran requested a call concerning comments on AC Briefing Document. Dr. Murphy & Dr. Gardner called Dr. Fadiran. Dr. Fadiran wanted to discuss various PK issues that he had on the Clinical Pharmacology document he had received.
12/01/98	Telecon with FDA	Re: Dr. Zimmerman looking for additional stability data from Brooklyn site. Roger Weaver called Dr. Zimmerman to discuss the stability package (request for 18 month data, possible shorter shelf life, PPI amendment issues). Dr. Zimmerman wanted to know when he would receive answers to his labeling questions from October 14 1998.
12/01/98	Request to FDA	Request for meeting to review final draft of Tikosyn AC Briefing Document.
12/02/98	Telecon with FDA	Dr. Chen (Medical Review Team Leader) wanted to discuss the maintenance of sinus rhythm data in the DIAMOND AF sub-study and for further ITT analysis.
12/02/98	Telecon with FDA	Dr. Fadiran (PK Reviewer) requesting additional drug capsule dissolution data.

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12/02/98	Telecon with FDA	Dr. Chen (Medical Review Team Leader) had questions about the QT/QTc data in the Integrated Summary of Safety. Later in the day Mr. Glen Andrews and Dr. Bill Murphy returned the call with answers.
12/02/98	FAX to FDA	Fax sent to Dr. Maryann Gordon. As discussed with Glen Andrews, materials for this afternoon's telecon (DRAFT: Corrections to Dr. Gordon's Safety Review, Received 11/6/98.
12/02/98	FAX to FDA	Fax sent to Dr. Charles Ganley. Additional information related to Dr. Ganley's October 22, 1998 queries.
12/03/98	Submission to FDA	Response to FDA Request for Information. Additional information re: Dr. Ganley's query on vital status of patients. Desk copy sent to Dr. Ganley.
12/03/98	Meeting with FDA	Pre-Advisory Committee Meeting with Division of Cardio-Renal Drug Products. Purpose of meeting: discuss updated draft of Briefing Document. Clinical Pharmacology and Efficacy sections were discussed. Dr. Lipicky commented and made suggestions on the structure of Briefing Document. Timing for submission of Briefing Document was discussed. Discussions were also around the DIAMOND studies. Dr. Fenichel briefly discussed the Division's philosophy on AC questions. Dr. Pratt asked about the composition of the AC and it was stated that there was a "large negative success rate." Next meeting with Division was discussed.
12/03/98	FAX to FDA	Fax sent to Dr. Shaw Chen with attached analyses on the maintenance of sinus rhythm for the patients for two DIAMOND studies. Draft data and final to follow.
12/04/98	FAX to FDA	Faxed to Ms. Standaert, Executive Secretary with request to have a discussion of Pfizer's logistical concerns with NIH staff.
12/04/98	FAX to FDA	Fax sent to Dr. MaryAnn Gordon with attached information regarding pre-clinical testicular evaluations (DRAFT).
12/04/98	FAX to FDA	Fax sent to Dr. Gordon with attached additional cuts of SAE ventricular arrhythmia data in the SVA population. Correction too information faxed on December 2, 1998 was included. (DRAFT information)
12/04/98	FAX to FDA	Fax sent to Dr. Gordon with preliminary (DRAFT) CYP 3A4 ketoconazole interaction study tables (watermark removed. Same fax went to Dr. Fadiran.
12/04/98	FAX to FDA	Fax sent to Dr. Emmanuel Fadiran with attached preliminary (DRAFT) CYP 3A4 ketoconazole interaction study tables (watermark removed).

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12/04/98	FAX to FDA	Fax sent to Dr. Chen with attached calculations used for percent change in QTC for NDA Tables and table revision request. Response is DRAFT with final to follow.
12/04/98	FAX to FDA	Fax sent to Dr. Gordon with attached preliminary (DRAFT) CYP 3A4 ketoconzole interaction study results.
12/04/98	FAX to FDA	Fax sent to Dr. Ganley with attached information regarding range of attacks which is DRAFT.
12/07/98	FAX to FDA	Fax sent to Dr. Akinwole Williams with attached minor discrepancies noted in Dr. Williams' draft review document and indicated by: *.
12/07/98	Telecon with FDA	Telecon with Dr. Chen to discuss the PowerPoint slides sent regarding AC Efficacy presentation slides. All AC Efficacy and Safety presentation slides will be sent to Dr. Chen electronically soon to facilitate his incorporating more of Pfizer's presentation slides into his review document.
12/07/98	Telecon with FDA (12/1, 12/2, 12/3 12/4)	Telecon of 12/1/98: with Mr. Roeder concerning CMC amendment was submitted to the NDA. Site issues in Puerto Rico were discussed. Telecon later with Dr. Gordon, Mr. Andrews, Dr. Mebus and Dr. Murphy concerning providing some additional data re: Safety Review. Telecon of 12/2/98: with Dr. Roeder and Dr. Murphy to follow-up and discuss new issues. Later in the day telecon with Dr. Friedrich, Dr. Roeder, Dr. Gordon and Dr. Murphy to discuss meeting to discuss preliminary results from dofetilide-ketoconazole interaction study. Telecon of 12/3/98: arrangements to meet were discussed and made. Telecon of 12/4/98: Ketoconazole interaction study data was provided to Drs. Gordon and Fadiran by FAX. Dr. Gordon requested to know when to expect the QT data.
12/07/98	Submission to FDA	Response to FDA Request for Information regarding stability information for mg capsules manufactured in Brooklyn.
12/08/98	FDA Correspondence	Requesting that the Division share the results of a study that would determine whether dofetilide is p-glycoprotein substrate Desk copy and requested drug sample was provided to Mr. Roeder.
12/08/98	FAX to FDA	Fax sent to Dr. Gordon with attached preliminary draft data from the CYP 2A4 ketoconazole interaction study. Same fax was sent to Dr. Fadiran.
12/10/98	Telecon with FDA (12/1, 12/2, 12/3, 12/4)	Telecon of 12/1/98: Mr. Andrews and Dr. Mebus called Dr. Gordon to discuss previous week's fax. Additional data was faxed 12/2/98. Telecon of 12/3/98: Dr. Gordon called Mr. Andrews to discuss previous day's fax. Mr. Andrews and Dr.

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		Friedrich returned the call a little later and she requested an additional table be sent which split proarrhythmias by dose. Telecon of 12/4/98: Follow-up to previous day's telecon and fax was sent with the splits she requested.
12/10/98	FAX to FDA	Fax to Dr. Gordon with attached draft of requested clarification regarding baseline in 115-023 study report.
12/10/98	FAX to FDA	Fax to Dr. Fadiran with attached requested assay validation reports for plasma and urine in study 115-201. Reports are referenced in the PK data for study 115-201.
12/11/98	Telecon with FDA (12/9 & 12/10/98)	Telecon with Ms. Joan Standaert, Terry Fisher (NIH) and Dr. Scaros. Logistical issues around AC meeting were discussed.
12/11/98	FAX to FDA	Fax sent to Dr. Zimmerman with attached final responses to last two questions of 10/7/98 fax. Typographical error to response to "Question Number 7" is also noted.
12/11/98	Telecon with FDA (12/4 & 12/10)	12/4/98: Mr. Roeder and Dr. Murphy discussed 11/23/98 CMC amendment and left message for Dr. Zimmerman to call. Dr. Zimmerman returned phone call on 12/4/98. Amendment and site issues were discussed. Telecon of 12/10/98: Questions were discussed that were received by fax and were forwarded to the appropriate RRT members.
12/14/98	Submission to FDA	Re: response to FDA request for information (Dr. Zimmerman). Final responses to labeling queries enclosed. Response to Dr. Gordon's request for info on a study report re: #115-203 sent by FAX on 12/10/98. Enclosure 2 is final response.
12/14/98	FAX from FDA	Dr. Gordon requesting clarification of baseline info for #115-203. Mr. Roeder called to relay request from Dr. Fadiran for info validating the assay used to measure urine and plasma dofetilide in #115-201. Requests passed to appropriate RRT members. (Gordon FAX attached)
12/14/98	FDA Log	FAX from Mr. Roeder: Cardio-Renal Division minutes. Minutes discuss best way to present dofetilide clinical clinical package at AC. Pfizer minutes parallel FDA minutes.
12/14/98	Telecon with FDA (12/9/98)	Telecon: Dr. Murphy, Dr. K. Williams, Dr. Marchant, Mr. Hilton and Dr. Akinowole Williams. Discussion of DIAMOND review. Request from Dr. A. Williams was faxed annotations for his review.
12/14/98	FDA Correspondence	Re: enclosed is the current draft version of the Tikosyn AC Briefing document. Twelve (12) desk copies to Mr. Roeder for distribution to Division staff.

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12/14/98	Telecon with FDA (12/8/98)	Telecon: Dr. Mr. And Dr. Fadiran. Requested Pfizer provide dissolution data in two other media. Dec. 8, 1998: Dr. Murphy and Dr. Weaver with Dr. Fadiran to discuss pellicle formation in dofetilide capsule, low dissolutions, and stability effects. Dr. Murphy offered a meeting with the Division.
12/15/98	Telecons with FDA (12/7, 12/8, 12/9, 12/11/98)	Draft PK data from ketoconazole interaction study sent to FDA on 12/4/98 and meeting to discussed scheduled. Dec. 7, 1998: Mr. Roeder called to say that Dr. Lipicky did not think a meeting necessary. Dec. 8, 1998: PD data from ketoconzole study provided to Drs. Gordon and Fadiran by FAX. Dr. Fadiran and Dr. Murphy discussed study results, offered Division to meet. Dec. 9, 1998: Telecon scheduled. Dec. 11, 1998: Availability confirmed by Division.
12/15/98	Telecon with FDA (12/10/98)	Telecon: Dr. Ganley, Mr. Andrews and Dr. Marchant. Patient information request.
12/21/98	FDA Correspondence	Re: response to FDA request for information. Enclosure 1: info requested by Dr. Ganley for study 115-365. Enclosure 2: info requested by Dr. Gordon, NDA info. Enclosure 3: request from Dr. Fadiran, assay validation data. No difference between draft and final responses. Desk copies to Drs. Fadiran, Gordon and Ganley.
12/22/98	FDA Log (12/17 and 12/21/98)	Dec. 17, 1998: FAX from Dr. Gordon re: briefing document. Dec. 21, 1998: Point corrected in the briefing document.
12/22/98	FDA Log	Fax from Mr. Roeder: FDA minutes from Nov. 23, 1998 received and parallel Pfizer's.
12/22/98	Telecons with FDA (12/16 and 12/17/98)	Dec. 16, 1998: Mr. Roeder said initial review of NDA done. Dec. 17, 1998: Division's package received (not distributed with log due to size).
12/23/98	FDA Log	FAX from Ms. Standaert. Supplemental list of AC participants and clarification of member list.
12/23/98	FDA Log	FAX from Dr. Gordon: request for additional info re: subjects included in NDA table. RRT personnel notified.
12/24/98	FDA Correspondence	Re: response to FDA request for information. DIAMOND study information.
12/24/98	FAX to FDA	To Dr. Chen. Summary SAE tables requested. Draft.
12/24/98	FAX to FDA	To Dr. Chen. Response to request for info for patients with lab abnormalities.
12/24/98	FAX to FDA	To Mr. Roeder: requests for two meetings.

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01/04/99	FDA Correspondence	Re: request for meeting to discuss prep for AC meeting. Additional meeting with Dr. Lipicky is requested.
01/05/99	FDA Log	Pre-AC meeting held with Cardio-Renal Division. Purpose to discuss briefing document. Panel and consultant clarification.
01/05/99	Telecon with FDA (12/18/98)	Telecon with Dr. Zimmerman. Site and amendment issues.
01/06/99	FAX to FDA	To Dr. Zimmerman, draft of dofetilide amendment 11/23/98 and FDA queries 12/10/98.
01/06/99	Telecons with FDA (12/23, 24/98)	Dec. 23, 1998: Called Mr. Roeder to discuss having a meeting. Dec. 24, 1998: Meeting agreed to and draft letter faxed.
01/06/99	Telecons with FDA (12/18, 24/98)	Dec. 18, 1998: Dr. Chen requested summary tables for SAE data. Called Dr. Chen back later with more info. Dec. 24, 1998: Voicemail left for Dr. Chen about requested tables.
01/07/99	FDA Log	Meeting with Cardio-Renal Division on Jan. 5, 1999. Meeting to discuss Tikosyn NDA and AC meeting.
01/07/99	FDA Log	Fax and correspondence with Mr. Roeder. Submit meeting request and draft letter faxed.
01/07/99	FDA Log	Phone conversation with Jeff Scaringe and Dr. Scaros. Discuss IT set-up for NIH Natcher Auditorium for AC.
01/07/99	FDA Correspondence	Propose revision to indication.
01/07/99	FAX to FDA	Copy of cover letter and Enclosure 1 (CMC info) to Dr. Zimmerman.
01/08/99	FDA submission	AC Briefing Document is submitted with note that addendum will be sent in near future.
01/08/99	FAX to FDA	Dr. Lipicky's request for recent exploratory efficacy analyses of study 115-113 figures were sent to Dr. Lipicky.
01/11/99	FDA correspondence	Re: response to FDA request for information. Enclosure 1: final response to points re: relationship data between ISS tables. Enclosure 2: final responses to request queries on CMC amendment issues. Desk copies to reviewers.
01/12/99	FDA correspondence (Unofficial)	Desk copies to Mr. Roeder of Safety and Efficacy presentations for AC meeting.
01/12/99	Telecons with FDA (12/22 & 12/31/98,	Dec. 31 1999: Ms. Standaert left voicemail about CDER and consultants. Jan. 5, 1999: Returned Ms. Standaert's call and

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	1/5,1/6, 1/8/99)	discussed consultants and committee reviewer issues. Room at Natcher for Pfizer on day of AC. Jan. 6, 1999: Consultant issues. Call returned with questions re: Lipicky and Roden at AC. Jan. 8, 1999: Ms. Standaert returned call about Lipicky and Roden issues.
01/12/99	FDA Log	FAX from Mr. Roeder of Draft Advisory Committee questions.
01/13/99	Telecon with FDA (12/14/99)	Telecon with Division of Cardio-Renal to discuss #115-257 study.
01/13/99	Phone conversation	Dr. Scaros and Terry Fisher of NIH re: AC meeting at Natcher Auditorium. Logistical issues discussed
01/13/99	FDA Log	FAX from Mr. Roeder of Cardio-Renal Division's minutes of telecon on Dec. 14, 1998 to discuss preliminary PK data.
01/13/99	Telecons with FDA	Jan. 7, 1999: Mr. Roeder request time change for Jan. 15th mtg. Supply of slides to AC committee issues. Jan. 11, 1999: Called Mr. Roeder to discuss slide copy numbers. Meeting change, labeling issues and request for draft questions also discussed. Jan. 12, 1999: AC questions to be faxed labeling revisions.
01/13/99	Submission to FDA	Combined Annual Report for time period May 15, 1997 through Sept. 20, 1998.
01/14/99	Phone conversation	Dr. Scaros and Terry Fisher of NIH re: video broadcast and communication system issues.
01/14/99	Telecon with FDA	Jan. 11, 1999 with Ms. Standaert re: panel issues.
01/15/99	Telecons with FDA (1/7, 11/99)	1/7/99: Call from Dr. Zimmerman re: draft response received and clarify points of his review. 1/11/99: Mr. Freeman, Mr. Buriak, Ms. Bickart and Dr. Murphy called Dr. Zimmerman to discuss these issues.
01/16/99	FDA Log	Copy of Dr. Chen's draft review (attached).
01/20/99	FDA Log	Pre-AC meeting with Division of Cardio-Renal. Discussion of draft AC questions.
01/21/99	Telecon with FDA (1/21/99)	Ms. Standaert request for agenda outlining Pfizer presentations for AC meeting. Due date of 1/22/99. Request for presentation slides to committee.
01/21/99	FAX to FDA	Info on 120 study ECG's to Dr. Chen (draft).
01/21/99	FDA Submission	Enclosure 1: addendum to briefing document. Enclosure 2: synopsis of study #115-016.

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		Enclosure 3: synopsis of study #115-257. Desk copies to Fadiran and 15 to Mr. Roeder for FDA distribution.
01/21/99	FAX from FDA	Minutes received from the Jan. 5, 1999 meeting. Minutes are consistent with Pfizer's minutes from the meeting.
01/21/99	Telecons with FDA (1/19 and 1/20/99)	1/19/99: with Dr. Chen to discuss DIAMOND trial issue and minor changes to Chen's review were made by same. 1/20/99: Revised version of Secondary Medical Review received and attached.
01/22/99	Telecon with FDA (1/14, 19, 20/99)	1/14/99: Dr. Zimmerman left voicemail re: sending additional CMC questions (FAX). Distributed to RRT. 1/19/99: Dr. Murphy left voicemail with Dr. Zimmerman explaining response timeframe. 1/20/99: Response time acceptable to Dr. Zimmerman.
01/22/99	FAX to FDA	Slides on Torsade de Pointes and mortality in patients dosed appropriately for their renal function sent to Dr. Lipicky.
01/22/99	Submission to FDA	Re: response to FDA request for information. Request for PK report for fluconazole study 056-027. Submitted to files. Desk copy to Dr. Fadiran.
01/22/98	FAX to FDA	Agenda for AC meeting and list of consultants sent to Ms. Standaert.
01/25/99	Telecons with FDA (1/20 and 1/21/99)	1/20/99: Mr. Roeder left voicemail had not received copy of dofetilide Annual Report. Returned call with explanation why attachment omitted. 1/21/99: Letter sent to both INDs and the NDA explaining the Annual Report submitted to the Oral IND and outline of proper cross reference.
01/25/99	FDA Log	FAX from Mr. Roeder of Final AC questions.
01/25/99	FDA Log	FAX from Mr. Roeder providing comments on proposed package insert.
01/25/99	Submission to FDA	Re: Information amendment, pharmacology/toxicology. Enclosure 1: draft tox report (98-642-02). Enclosure 2: references to draft study report (98-642-02). Enclosure 3: genetic tox report. Enclosure 4: references for draft study report (98-643-04). Desk copies to Drs. Gill-Kumar and Resnick.
01/26/99	Telecons with FDA (1/13, 14, 15, 20, 21/99)	Jan. 13 & 14, 1999: Dr. Ganley left voicemail about study transport file with ECG info. 1/15/99: Mr. Andrews called Dr. Ganley to clarify his query and discuss SAS files. 1/20/99: Call to Dr. Ganley to discuss patients with AF relapse endpoint in study 120. Jan. 21, 1999: Table and memo of eval of endpoints faxed to Dr. Ganley.

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01/27/99	Submission to FDA	Re: Submission of Annual Report on 1/13/99.
01/27/99	Submission to FDA	Re: CMC amendment, environmental analysis issues with attachments. Attachment 1: Pfizer authorized rep of PPPCL. Attachment 2: second categorical exclusion from environmental analysis requirements.
2/3/99	FAX from FDA	On 1/29/99, a FAX of the FDA's Minutes to the 12/21/98 meeting re: Advisory Committee Preparation
2/3/99	FAX from FDA	On 1/29/99 a FAX was received with Dr. Pritam Gill-Kumar's comments on the proposed PI. His comments pertain to "Carcinogenesis, Mutagenesis, Impairment of Fertility", "Pregnancy Category" and "Clinical Pharmacology" section of the label
2/3/99	FAX to FDA	FAX to Dr. Zimmerman of final responses to his queries from 1/14/99 re: Blister Usage Issue, Stability/Dissolution Data , 500 Bottle count, packaging and labeling issues
2/3/99	Submission to FDA	Attachment 1: Response to Dr. Lipicky's query for initial results of recent exploratory efficacy analyses from study 115-113[1] from the 1/5/99 pre-Advisory Committee meeting. Enclosure 2: response for additional Chemistry manufacturing and Controls information as requested by Dr. Zimmerman on 1/14/99 by FAX
2/8/99	FAX to FDA	Faxed current working draft of PI (version 2/8/99) to FDA
2/9/99	FAX to FDA	FAX to Dr. Stuart Zimmerman of the "Description" and "How Supplied" sections from the current draft of Tikosyn USPI. Pfizer's query response of 2/3/99 is reflected in the proposed draft USPI
2/9/99	FAX from FDA	Mr. Roeder faxed a copy of the Pletal (cistazol) PPI for Pfizer to use as a model. Pletal was the most recent PPI the Division reviewed.
2/10/99	Submission to FDA	Enclosure 1: formal submission to Dr. Gordon's request for PID numbers listed in Table H.6.13.9 of the NDA; Enclosure 2: working draft of PI includes new information not available at the time of the initial NDA. The "How Supplied" section of the working draft has been updated since the FAX on 2/8/99.
2/11/99	FAX to FDA	re: Dr. Gill-Kumar's request for copies of two publications referenced in the NDA
2/11/99	FAX to FDA	re: Pfizer's request for Dr. Gill-Kumar to reconsider revisions to pharmacology labeling and supporting publications

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BRIEF DESCRIPTION OF REPRESENTATIVE MAJOR ACTIVITIES
DURING THE REGULATORY REVIEW PERIOD

DATE	ACTIVITY	COMMENTS
2/11/99	FAX from FDA	re: FDA minutes to the 1/15/99 meeting about Advisory Committee Preparation
2/12/99	Telecons with FDA (2/1, 2, 3, 5, 8, 9/99)	re: Division sent their revised version of the PI to Dr. Temple, FDA requested a working draft of the PPI; timelines for the PI and PPI were discussed; the "How Supplied section of the label did not reflect a revision made to the NDA on 2/3/99 therefore an updated version of the PI was sent to Mr. Roeder via secure e-mail.
2/12/99	Submission to FDA	re: query from Dr. Pritam Gill-Kumar (Pharmacology Reviewer) for two publication referenced in the NDA; Enclosure 1: the two manuscripts that were faxed on 2/11/99 to Dr. Gill-Kumar; Enclosure 2: Pfizer's request to Dr. Gill-Kumar to reconsider some edits to the proposed PI.
2/12/99	FAX to FDA	re: source tables for Tables 3 and 4 in the working draft of the Tikosyn package insert for Dr. MaryAnn Gordon
2/15/99	Telecons with FDA (2/9, 11, 12/99)	re: Dr. Gordon's inquiry for supporting data from the NDA for the PI; She requested final SAS tables supporting the tables 3 and 4 in the PI. Final SAS output was sent faxed to the FDA on 2/12/99.
2/18/99	Telecons with FDA (2/11, 12/99)	re: upcoming meeting with CDER management; FDA inquiry if Pfizer had a marketing plan and made recommendations for Pfizer's marketing plan. FDA sent Pfizer revisions to the PI and asked that Pfizer not react until Dr. Temple's have been received.
2/22/99	Telecon with FDA (2/18/99)	Dr. Zimmerman left voicemail re: storage conditions statement in the working draft of the PI; may be necessary to submit new labeling. A call was returned to him indicating a response to his query would be submitted as soon as possible and inspection of the Puerto Rico production site was completed which would resolve the last major CMC issue
2/22/99	Telecons with FDA (2/9, 10, 11, 12, 16, 17, 18/99)	re: Dr. Gill-Kumar's raised several points about the package insert. Issues are detailed in her review of the NDA; Upon receipt of this document, several telecons have occurred. Attachment: FAX from FDA with comments on the NDA from the Pharmacologist, Dr. Gill-Kumar.
2/22/99	Submission to FDA	Response to Dr. Grines unanswered question during the Tikosyn AC meeting re: discontinuation due to objective test findings in the dofetilide and quinidine groups.
2/23/99	Telecons with FDA (2/17, 19/99)	The Division would like to review the Tikosyn Marketing plan as soon as possible. Dr. Temple is in the process of revising the PI. Mr. Roeder said Pfizer should be prepared to

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		address a point Dr. Fenichel would suggest a strict approach (e.g., intense physician education, limited distribution)
2/23/99	FAX from FDA	FAX on 2/12/99 from Dr. Lipicky and the Reviewers in the Cardio-Renal Division 's comments to the Working draft of PI submitted to FDA on 2/8/99. FDA agreed to provide Pfizer with the revisions and any negotiations would not begin until Dr. Temple's comments were incorporated into the draft.
2/24/99	Telecons with FDA (2/23, 24/99)	2/23/99 Ms. Wittich (DRAD, NY) and Dr. Murphy called Mr. Roeder to discuss objectives of the upcoming March 1st meeting with the Cardio-Renal Division and Drs. Temple and Woodcock. Issues would dictate the Pfizer attendees, Pfizer wants to insure the appropriate people attend. On 2/24/99 Mr. Roeder spoke with Dr. Lipicky re: labeling being discussed at the March 1st meeting and Dr. Lipicky suggested Pfizer be prepared and have the appropriate people at the meeting.
2/24/99	FAX to FDA	Faxed to Dr. Temple re: draft of Tikosyn plan for initial commercialization; provided as background for meeting on 3/1/99 with Drs. Temple and Woodcock.
2/24/99	FAX to FDA	Faxed to Mr. Roeder re: draft of Tikosyn plan for initial commercialization; provided as background for meeting on 3/1/99 with Drs. Temple and Woodcock.
2/24/99	Submission to FDA	Information Amendment - Pharmacology/Toxicology Enclosure 1: Study 98-642-02 Genetic Toxicology Report, Enclosure 2: Reverences for study report 98-642-02, Enclosure 3: Study 98-642-04 Genetic Toxicology Report, and Enclosure 4: References for study report 98-642-04
2/26/99	FAX to FDA	Copy of study report to provide background during 3/2/99 telecon with Drs. Gill-Kumar and Resnick re: review the safety margins concerning dofetilide-induced testicular atrophy in the dog Attachment: "Examination of Sections of Testis and Epididymis from Two Toxicity Studies Conducted in Beagle Dogs"
2/26/99	FAX from FDA	Draft comments from Dr. Lipicky on approvability of NDA 20-931 Summary states Dofetilide should be approved and provided mark up versions of the PI and PPI.
3/1/99	Submission to FDA	re: response to request from Dr. Maryann Gordon for data supporting the 2/8/99 working draft PI tables 3 and 4
3/2/99	FAX to FDA	Final response to Dr. Fadiran's comments re: dissolution issues
3/3/99	Submission to FDA	Response to support analyses presented in the Tikosyn AC Briefing Document submitted to the NDA on 1/8/99. Enclosure

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		1: Information on one year survival from first dose of study drug for studies 120 and 345. Enclosure 2: maintenance of sinus rhythm for patients who received lower dose than their randomized dose in studies 120 and 345. Enclosure 3: final version of the safety review includes factual corrections to discrepancies previously submitted to Dr. Gordon of the FDA Enclosure 4: Summary Serious Adverse Events tables Enclosure 5: Response to Dr. Fadiran's review comments and issues
3/3/99	FAX to FDA	Slides #25 and 26 re: Oral placebo-controlled trials: Torsades De Pointes and Oral placebo-controlled trials: TdP Before and After CLCr Amendment
3/4/99	FAX to FDA	FAX sent to Dr. Zimmerman re: storage conditions, stability Protocol for Commercial Dofetilide, dissolution, and response to Dr. Fadiran's queries.
3/4/99	Telecons with FDA (2/22, 23 & 3/1, 2, 3/99)	Dr. Zimmerman concerned with the storage conditions statement in the working draft of the PI. Dr. Casey of Pfizer satisfactorily resolved the issues with Dr. Zimmerman.
3/4/99	Telecons with FDA (2/26/99, 3/3/99)	re: omission noted in the DIAMOND MI study report table; Mr. Roeder requests the complete table be added to the electronic submission and to update the electronic archive.
3/4/99	FAX to FDA	Two pages(modified per telecon) faxed to Dr. Zimmerman re: Stability for Protocol for Commercial Dofetilide Capsules and Dissolution sent from Dennis Casey of Dev. Research at Pfizer
3/4/99	Submission to FDA	re: query from Dr. Zimmerman; final response (supercedes previous response) on CMC issues re: storage conditions
3/8/99	FAX to FDA	Dr. Murphy provides Dr. Gill-Kumar the location of the study report supporting the mouse plasma protein binding statement in the NDA (both hard copy and Esub). Attachment: Cover page of the study report for Dr. Gill-Kumar
3/11/99	FAX from FDA	On 3/5/99, FAX was received of the Division's approvable letter of Tikosyn and draft labeling.
3/11/99	Submission to FDA	Response to FDA's request for updated Appendix V, Table 11 to both the electronic submission tool and the NDA archive for study report #115-400 MI DIAMOND.
3/12/99	Submission to FDA	Pfizer acknowledges approvable letter re: NDA 20-931. Division is informed of Pfizer's intent to file and amendment to NDA 20-931 to address points raised in the approvable letter dated 3/5/99. Attachment: Amendment to pending NDA.
3/12/99	Submission to FDA	Submitted final synopsis report for study 115-016

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3/16/99	Meeting with FDA (3/1/99)	3/1/99 meeting re: Tikosyn commercialization plan, Dr. Temple wants to approve Tikosyn under Subpart H. Another meeting will be scheduled to discuss commercialization and Subpart H following the approvable letter
3/19/99	Telecon with FDA (3/11/99)	Dr. Murphy confirmed with Mr. Roeder that the 3/5/99 Tikosyn approvable letter which contained statements re: promotional materials; the Division did not expect Pfizer to provide the materials at this time.
3/19/99	Telecons with FDA (3/8, 16/99)	re: The 3/5/99 Tikosyn approvable letter noted an additional meeting was necessary to discuss the proposed marketing and distribution plan. Dr. Murphy and Mr. Roeder tentatively agreed to the meeting schedule.
3/19/99	Telecons with FDA (3/11, 16/99)	3/11/99 Dr. Fenichel suggested Pfizer consider presentation of dose in the PI be in micrograms rather than milligrams. His thought is that whole numbers are simpler for both Physician and Pharmacist. It was mentioned that Pfizer discussed milligram vs. microgram with the FDA prior to submitting the NDA. 3/16/99 Mr. Roeder said Dr. Temple agreed doses in the PI should be expressed in whole numbers.
3/19/99	Submission to FDA	re: Submission on 3/11/99 of an updated study report table (study report 115-400 MI, Appendix V, Table 11) Corrected information to the inaccuracies noted in the cover letter statement regarding compliance to FDA's "Guidance for Industry, Providing Regulatory Submissions in Electronic Format - NDAs"
3/22/99	Telecons with FDA (3/5, 10, 16/99)	Issues re: dissolution testing of Tikosyn previously discussed with Dr. Fadiran on 12/14/98. Prior to issuing the Tikosyn approvable letter, Drs. Fadiran and Marroum wanted to revisit the topic with Pfizer. It was requested that any new information referenced in the document, must be formally submitted to the NDA. Tikosyn would be approved on an interim dissolution specification.
3/22/99	Telecon with FDA (3/16/99)	3/16/99 re: clarification about the serious arrythmias table for DIAMOND AF patients in the revised Tikosyn PI
3/26/99	FAX from FDA	FDA minutes from Pfizer's meeting with the FDA on 3/1/99 re: Marketing and Distribution of Tikosyn
3/29/99	Telecons with FDA (3/4, 16/99)	3/4/99 re: final Pharmacology issue, Dr. Gill-Kumar restated her position that 0.1 mg/kg/day was the NOAED (no observed adverse effect dose) in the dog. On 3/16/99 FDA's minutes to the 3/4/99 telecon were received.
3/30/99	Telecons with FDA (3/19, 23, 25, 29/99)	Pfizer inquired if FDA Chemistry team should be invited to Pfizer's meeting with FDA Biopharmaceutics Reviewers.

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		Other telecons were to schedule meeting with Drs. Marroum and Fadiran and confirmation of the meeting time on 4/7/99.
4/6/99	Telecons with FDA (3/3, 4/99)	4/3/99 Telecon with Dr. Zimmerman to resolve all CMC issues prior to the FDA's approvable action letter. Mr. Zimmerman agreed if all issues discussed were submitted in writing; all CMC issues would be resolved and taken out of the FDA approvable letter. He would also report this to the Division during a meeting on 3/4/99.
4/9/99	Submission to FDA	Two slide sets (all core and backup) from the Tikosyn AC meeting on 1/28/99 are being provided to Mr. Roeder and Mr. J. Treacy.
4/20/99	Telecons with FDA (4/15, 19/99)	4/15/99 discussed agenda for upcoming Cardio-Renal AC meeting on 4/30/99. Assurance was given that the Division would not present any dofetilide data without conferring with the Sponsor. 4/19/99 Mr. Roeder agreed to review the pre-meeting package for any specific dofetilide data as per Dr. Murphy's request.
4/23/99	Submission to FDA	Response to Dr. Robert Fenichel's request on 1/15/99 re: if the effect of concomitant medication s on QT variation in subjects have been examined.
4/29/99	Submission to FDA	Enclosure 1: revised package insert, version 4/28/99 (result of Divisional comments on PI in 3/5/99 approvable letter). Enclosure 2: "revision-mode" (strike-through) version. Enclosure 3: Electronic copies of enclosures 1 and 2.
5/3/99	Submission to FDA	Letter to follow-up discussions between Pfizer and the FDA concerning pending NDA; re classification of Tikosyn as "Subpart H" per CFR 314.520. Pfizer firmly opposes Subpart H approval of Tikosyn.
5/11/99	Telecons with FDA (5/7, 10/99)	In-house evaluation of dofetilide on the p-GP were submitted to the FDA on 9/9/98. 5/7/99 Telecon Dr. Fadiran of FDA requests to submit an abstract for publishing. Dr. Murphy requests a copy of the abstract for our internal review process. Dr. Fadiran concluded that dofetilide is not a substrate for p-GP. 5/10/99: FAX of abstract was received from Dr. Fadiran.
5/12/99	Meeting with FDA (4/7/99)	4/7/99 Meeting: In the 3/5/99 approvable letter Tikosyn was approved on interim dissolution test specifications. Pfizer met with Biopharmaceutics reviewers to discuss the dissolution specifications. Meeting concluded with a compromise whereas Pfizer would submit an experimental protocol to evaluate possible alternative dissolution test methods and/or criteria. On 4/21/99 Fax received from FDA of the meeting minutes from 4/7/99.

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5/14/99	Telecons with FDA (5/6, 11, 13/99)	05/06/99: Mr. Roeder requests to cancel meeting on 5/7/99 and Dr. Temple continues to review Pfizer's May 3rd letter to FDA on Subpart H. 5/11/99 Telecon: re: package insert and action concerning Subpart H. Mr. Roeder added that a request to present dose in milligram vs. microgram may be forthcoming. 5/13/99: Pfizer prefers to use micrograms to milligrams since poison control markings on capsules will be in whole numbers and market tests indicate physicians prefer to use whole numbers.
5/14/99	Telecons with FDA (5/13, 14/99)	05/13/99: Dr. Gordon of FDA requested clarification on PI, page 10, Table 3 re: TdP under the 250mcg BID dose. If true, this would increase rate of TdP in the SVA population to .9%. The second query referred to pg. 10 and TdP in the SVA population. FDA questioned if the number of patients dosed correct according to the dosing algorithm. Pfizer provided answer to FDA's queries. 5/14/99 telecon: Dr Gordon at FDA confirmed she received response to queries and said the PI was too long and redundant. She would continue to review the PI and call with any additional queries
05/21/99	Submission to FDA	re: approvable letter from FDA on March 5, 1999 and request for Pfizer to provide additional dissolution data in several additional media. Attachment 1: Pfizer minutes to meeting with FDA on April 7, 1999. Attachment 2: Slides presented by Pfizer at the 4/7/99 meeting. Pfizer requests clarification from FDA on "an appropriately discriminating dissolution method."
5/26/99	Telecons with FDA (5/19, 21/99)	5/19/99: re: milligram vs. microgram issue. FDA would probably agree with Pfizer on the issue 5/21/99: Pfizer preferred to present doses in micrograms. Dr. Temple would accept if doses are in both microgram and milligram. Expected time for Comments from FDA on PI were discussed. Dr. Murphy mentions that because FDA requested for a sentence to be deleted under "Clinical Pharmacology-Electrophysiology" a sentence should be added re: ERP in atrial tissue. He points out that the PI makes reference to HIS-Purkinje system and the ventricles, but not to the effects on the atria. A request to the NDA for this addition to the PI will be sent.
5/28/99	Submission to FDA	Pfizer requests additional information be added to PI re: Tikosyn on the effective refractory period in atrial tissue
6/7/99	Telecons with FDA (6/1, 4/99)	6/1/99: Dr. Murphy asks if FDA has reviewed PI submitted on 4/29/99. On 6/4/99 Dr. Roeder states there is no new information on PI and would contact Dr. Murphy with any new information.
6/15/99	Letter from FDA	Comments from the FDA response to May 3rd letter from Dr. Cheryl Graham re: Subpart H and Labeling.

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6/24/99	Telecons with FDA (6/14, 15, 17, 18/99)	6/14/99: Dr. Temple's comments on USPI would be faxed to Pfizer on 6/14/99. 6/15/99: Comments on USPI would be sent in two separate faxes. Remaining issues re: labeling and the Black Box warning would be discussed later as well as request for PPI or Medguide. 6/17/99: Reviewers request for PPI in Medguide format. A meeting would be scheduled for 6/21/99 to discuss alternate dosing recommendation and "unit of use packaging." 6/18/99: Telecon scheduled for 7/7/99 was confirmed. Pfizer USPI must be submitted by 6/30/99. Division draft of PPI may be available by 7/7/99 telecon. 6/15/99 FAX received from FDA of draft PI with Dr. Temple's comments. 6/15/99: A Second FAX from the FDA included comments on Subpart H and Labeling. 6/17/99: FAX from FDA of additional labeling comments re: Precautions: use in Female Patients.
6/24/99	Submission to FDA	Pfizer request to FDA that Pfizer data for Tikosyn 345 study not be considered in support of Berlex NDA approval. Pfizer's data was presented at Berlex's AC meeting on 4/30/99
7/7/99	Telecons with FDA (6/29 & 7/1/99)	6/29/99: Mr. Roeder called to discuss revised PI and scheduled time for telecon on 7/7/99. 7/1/99: Dr. Murphy called Mr. Roeder to review FDA participants for 7/7/99 telecon and discuss timing of future telecons to discuss PPI and USPI issues. Mr. Roeder requested to reschedule the 7/7/99 telecon.
7/7/99	Submission to FDA	Pfizer's response to FDA comments on PI received on 6/15/99 Enclosure 1: revised PI version dated 7/2/99, Enclosure 2: A revision mode (strike-through) version of the document, Enclosure 3: Electronic copy of enclosure 1 and 2 for Mr. Roeder. Enclosure 4: Copy of the Tikosyn Education/Distribution Program.
7/8/99	Telecon &Facsimiles with FDA (6/21 & 7/2/99)	6/21/99 Telecon: Pfizer agrees with FDA to add language to the PI for Physician's to use lower dose than 500 mcg BID. FDA says "Black Box" to remain in PI. FDA requires all Tikosyn bottles to have the PPI. FDA, DDMAC, and Pfizer to work on PPI. 6/21/99: FAX received from FDA with comments on PPI. 7/2/99 FAX received from FDA of the minutes of the 06/21/99 Telecon.
07/22/99	Telecons & Facsimiles with FDA (7/12, 13, 15, 16/99)	07/12/99 Telecon: Dr. Murphy requests status of PI review by the FDA. 7/13/99 FAX from FDA includes PI with FDA comments. 7/13/99 Telecon re: rationale for remaining in normal sinus rhythm, Table 2, Diamond CHF, Education/Distribution in the How supplied section, Dosage Administration or Warnings. Discussed deferral or waiver to Pediatric Rule.

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		7/14/99 FAX received with FDA comments re: AF/AFI , Special Considerations under Dosage and Administration. DDMAC to comment on PPI and take into consideration Dr. Temple's comments. 7/15/99 deferral or waiver of Pediatric Rule 7/16/99 Working draft of PI was faxed to the FDA and would be the basis of discussion on 7/19/99.
7/23/99	Telecons with FDA (7/20, 21/99)	7/20/99: Dr. Murphy called Mr. Roeder to discuss FDA's request for all DIAMOND MI all-cause hospitalization and hospitalization for worsening heart failure be added to PI. FDA suggests to approve Tikosyn under a deferral for Pediatric Rule. 7/21/99 Mr. Roeder called Dr. Murphy re: DIAMOND MI hospitalization information; DDMAC had completed review of PPI which would be sent to Pfizer on 7/26/99; he asked for expected time of the final version of PI.
07/28/99	Telecon with FDA (7/14/99)	re: revised PI dated 7/7/99 including: How Supplied, Dosage Administration, Clinical Pharmacology, Indications and Usage Warning, Ventricular Arrhythmia, Frequency of TdP, Precautions, other Drug Interaction Information, Digoxin, Adverse Reactions, Other Adverse Reactions, Dosage and Administration, and Special Considerations.
07/28/99	Telecon with FDA (7/19/99)	re: Two main issues of PI resolved including wording of maintenance of normal sinus rhythm indication and special considerations under Dosage and Administration; Pediatric Rule requirements to be addressed post-approval.
07/30/99	Telecons with FDA (7/12, 14, 19/99)	re: Changes to Methods Validation and dissolution and request for Pfizer contact of CMC.
07/30/99	FDA Log	E-mail from Mr. Roeder with a revised PPI including DDMAC's and Dr. Temple's comments. Attachment: Working Draft of PPI.
08/10/99	FAX from FDA	FDA minutes of the teleconferences on July 14 & 19, re: labeling and PPI.
08/19/99	Telecons with FDA (8/12, 13/99)	FDA Confirmed receipt of new PPI wording. Discussed specifics re: final NDA submission (final package insert, PPI and container labels). Attachment 1: "What is the most important information I should know about Tikosyn?"
08/25/99	Telecon with FDA (8/11/99)	FDA comments on the PPI submitted by Pfizer. Attachment 1: Working draft version dated 7/29/99 of PI. Attachment 2: "What is the most important information I should know about Tikosyn?"

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08/25/99	Telecons with FDA (8/18, 19/99)	FDA requested update on the PPI, is working on the approval letter and has no issues at the present time. Scheduled meeting for 9/1/99 to discuss Pfizer PPI with the FDA.
08/30/99	Submission to FDA	Revised Working draft of the PPI includes draft proposal of "What is the Most Important Information About Tikosyn?"
9/2/99	FAX from FDA	FDA minutes of the telecon on 8/11/99 re: Patient Package Insert; includes working draft version dated 7/29/99 with FDA comments.
9/8/99	Submission to FDA	Final printed Tikosyn PI includes revisions discussed in previous telecons as requested by FDA; Enclosure: twenty sets of Tikosyn carton and container labels, ten sets of labels mounted on heavy paper, and packaging materials provided for each of the three Tikosyn dosage forms. Issues re: the PPI have been incorporated and the final version is undergoing review and will be submitted to the Division in the near future.
9/15/99	Submission to FDA	Submitted final draft version of PPI and copy of previous version submitted on 8/30/99.
9/16/99	Submission to FDA	re: Provided FDA with an electronic version of the final Tikosyn PI; Enclosure 1: one CD Rom.
9/17/99	Telecon with FDA	The Tikosyn NDA is undergoing final review and sign-off within the Division.
9/22/99	Fax from FDA	FDA's Minutes of the telecon Sept. 1, 1999 regarding the Patient Package Insert.
10/1/99	Fax from FDA	Approval letter from Dr. Robert Temple.